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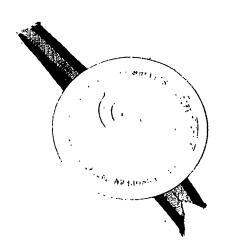
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Der Präsident des Europäischen Patentamts Im Auftrag For the President of the European Patent Office Le Président de l'Office européen des brevets

Cristina lacoponi

Patentanmeldung Nr. Patent application no. Demande de brevet nº

PCT/EP 04/004891

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COMPOSITION OF PROTEIN COMPLEXES ASSOCIATED WITH THE METABOLISM OF APP AND THE AB-PEPTIDES

1. FIELD OF THE INVENTION

The present invention relates to protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

2. BACKGROUND OF THE INVENTION (cited references are listed in supra)

Alzheimer's disease is a chronic condition that affects millions of individuals worldwide. After onset of the disease sufferers require a high degree of supervision and care. As the proportion of aged individuals in the population increases, the number of sufferers of Alzheimer's disease is expected to expand dramatically. Current top drugs (e.g. Aricept®/donepezil) attempt to achieve a temporary improvement of cognitive functions by inhibiting acetylcholinesterase, which results in increased levels of the neurotransmitter acetylcholine in the brain. These therapies are not suitable for later stages of the disease, they do not treat the underlying disease pathology, and they do not halt disease progression. The growing need for an effective therapy, coupled with the absence of effective treatments, presents a significant opportunity for drug target development and drug discovery.

The brains of sufferers of Alzheimer's disease show a characteristic pathology of prominent neuropathologic lesions, such as the initially intracellular neurofibrillary tangles (NFTs), and the extracellular amyloid-rich senile plaques. These lesions are associated with massive loss of populations of CNS neurons and their progression accompanies the clinical dementia associated with AD. The major component of amyloid plaques is the amyloid beta peptide. Amyloid beta is the proteolytic product of a precursor protein, beta amyloid precursor protein (beta-APP or APP). APP is a type-I trans-membrane protein which is cleaved by several different membrane-associated proteases. The first cleavage of APP occurs extracellularly by one of two proteases, alpha-secretase or beta-secretase. Beta-secretase or BACE1 (beta-site APP-cleaving enzyme) is a type-I

transmembrane protein containing an aspartyl protease activity (described in detail below). Alpha secretase is a metalloprotease whose activity is most likely to be provided by one or a combination of the proteins ADAM10 and ADAM17. Following either the beta or alpha cleavage of APP, the final cleavage event occurs within the membrane and is carried out by a protein complex called gamma secretase. It is the combination of the beta and gamma secretase activities that results in the liberation of the Abeta peptides of 40 and 42 residues (there are also lower levels of other forms) from the APP and ultimately the formation of the amyloid plaques responsible for the pathology of Alzheimer's disease. It is believed that the Abeta-42 peptide is the most critical Abeta species, because it shows the most pronounced neurotoxicity, and can aggregate easily, thus forming a nucleus for the aggregation of other Abeta peptides, such as the Abeta-40 which is typically produced at higher levels than the other species.

The applicant's proprietary proteomics technology (TAP/LC-MS/MS) is particularly successful in the elucidation of membrane protein complexes. These multiprotein complexes form the core of the APP processing pathway and are not amenable to other techniques. Known proteins with an important functional role in APP processing were analysed with The applicant's technology to comprehensively chart the dynamic protein interactions that contribute to Abeta production. Selected novel targets are subsequently validated using cellular or biochemical assays. Moreover, purified multi-protein complexes (e.g. beta- or gamma-secretase) do represent defined functional molecular machines, which are used to evaluate the mechanism of known compounds and for the optimisation of leads.

<u>Presenilins</u>

Presentilins 1 and 2 (PS1 and PS2) are integral membrane proteins which are localised in the endoplasmic reticulum, the Golgi and also at the cell surface (1). They are predominantly found as a heterodimers of the NTF and CTF endoproteolytic fragments. The protease that cleaves presentlins (the "presentlinase") is not known, it is likely that the process is autocatalytic, also the functional significance of PS (auto)proteolysis is unclear.

Presenilins are involved in the proteolytical processing of Amyloid precursor protein (APP) (2,3) and the Notch receptor (4,5). In addition, Presenilins are associated

with the cell-adhesion proteins alpha and beta-catenin, N-cadherin, and E-cadherin (6) (7) and other members of the armadillo family (8) (9) (10) (11).

APP processing by Presenilins is through their effects on gamma-secretase which cleaves APP, generating the C-terminus of the A-beta peptide. PS1 associates with the C83 and C99 processed C-terminal fragments of APP (12), Nicastrin (13) and Pen-2 (14). Aph-1 (15) (14) is required in Presenilin processing. It is not clear whether Presenilins regulate gamma-secretase activity directly or whether they are protease enzymes themselves (16). The gamma-secretase activity could comprise a multimeric complex of these proteins (13) (17) but it is not known how the relationship between these proteins affects secretase activity.

Familial Alzheimer's disease (FAD) patients carry mutations in the presentilin proteins (PS1; PS2) or in APP. These mutations result in increased production of Abeta42 (18) which is the main component of cerebral plaques in FAD (19).

Understanding the composition of the gamma-secretase complex, the relationship between its component parts and its regulation are important in the design of drugs for use in Alzheimer's disease patients.

<u>Nicastrin</u>

Nicastrin is a type 1 trans-membrane glycoprotein with a conserved transmembrane domain and DYIGS motif (13) which is constitutively expressed in neural cell lines (20). Biochemical studies have shown that Nicastrin binds to Presenilins 1 and 2, C-terminal derivatives of APP (13), membrane-tethered forms of Notch (21) and that it is a member of the gamma-secretase complex along with PS1 and PS2 (17). Gamma secretase activity is involved in the cleavage of both Notch and APP. It has been shown that Nicastrin is required for the intra-membrane cleavage of Notch (22) and APP (23), it may also have a role in post-translational stabilisation of Presenilin (24).

Aph-1 (15) and Pen-2 (14) were cloned recently in a screen for presentiin enhancers ("pen") in C. elegans and shown to interact genetically with Aph-2 (Nicastrin). Defects in Aph-1 affect Notch signalling and Nicastrin localisation (15). Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presentiins. Francis et al. (14) cloned the putative human orthologues of these genes, Aph-1a, Aph-1b and Pen-2, and recently Lee et al. (25) also cloned the human Aph-1 cDNAs.

The exact components of the gamma-secretase complex are not known but these two novel proteins could be components of or accessory factors to the complex and may interact together directly with Presenilin or with a Presenilin/Nicastrin complex. Nicastrin is therefore a member of the active gamma-secretase complex and there is recent evidence that it is the fully glycosylated form of the protein which is important in this complex. (26-30)

Aph-1

Goutte et al. (15) cloned aph-1 from C. elegans. Aph-1 encodes a novel conserved membrane protein with seven hydrophobic regions which are predicted to be membrane spanning. It has a 40 amino acid hydrophilic tail. C. elegans aph1 mutants have a phenotype which is indicative of a defect in Notch signalling. In these mutants, Aph-2 (Nicastrin) localisation is altered from being at the cell surface to being in the cytoplasm, concentrated around the nucleus. In C. elegans, Aph-1 interacts genetically with Aph-2 (Nicastrin) and Sel-12 (one of the C. elegans Presenilin genes) (14).

There are Human, Mouse, Drosophila Aph-1 homologues which are potential orthologues. Recently, the human Aph-1 homologues, hAph-1a and hAph-1b have been cloned (14,25). Aph-1a, the hypothetical CGI-78 protein, and Sambiasin (European Patent Application 02014244.4 are all products of the same gene. Francis et al (14) showed that Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presenilins in cultured Drosophila cells.

Lee et al. (25) cloned two splice variants of Aph-1a called Aph-1aS and Aph-1aL and Aph-1b. They have shown that mammalian Aph-1aL associates with Nicastrin and PS1 NTF/CTF heterodimers and with PS2 and Nicastrin in cultured cells and that endogenous Aph1aL associates with Nicastrin and PS1 in rat brain. Inhibition of the expression of Aph1a reduces the expression of both PS1 and PS2 but not Nicastrin and results in the accumulation of gamma-secretase substrates and the reduction of AbetaAph1a was also shown to be required for Notch cleavage.

Aph-1 may have a role in the maturation and trafficking of Nicastrin but it is necessary for gamma-secretase function and may be a member of the gamma-secretase complex.

Pen-2

Francis et al. (14) isolated pen-1 and pen-2 as two presentilin enhancer genes in a genetic screen in C. elegans. Pen-1 is identical to Aph-1 (15). Pen-2 has two transmembrane domains and is thought to be a polytopic integral membrane protein. This group cloned the human homologues of Aph-1 and Pen-2. In C. elegans, Aph-1 and Pen-2 interact genetically with Aph-2 (Nicastrin) but not with each other. Hop-1 and Sel-12 are the C.elegans presentlin genes. Aph-2 interacts with Hop-1 whereas Aph-1 and Pen-2 interact with Sel-12 (14).

Pen-2 associates with PS1, PS2 and Nicastrin in mammalian cells and Aph-1 and Pen-2 are required for Notch cleavage, gamma-secretase activity and the accumulation of processed Presentiins in cultured Drosophila cells (14).

Nicastrin maturation is affected by the levels of PS1 and Pen-2. Loss of PS1 or a reduction in expression of Nicastrin reduces Pen-2 protein levels and a reduction in expression of Pen-2 decreases levels of both PS1, PS2 proteins. In addition, reducing the expression of Pen-2 by RNAi reduces the level of the PS1 complex (31). These data suggest that Pen-2 is either a component of or regulates the assembly of the PS1 complex and that the expression of these proteins is co-ordinately regulated.

BACE1 (beta-secretase)

Vassar et al. (32) cloned a transmembrane aspartic protease that had the characteristics of the postulated beta-secretase of APP. Three other groups also cloned BACE1 using different approaches. BACE1 knockout mice have a normal phenotype, suggesting that therapeutic inhibition of BACE1 for AD may be free of mechanism-based toxicity. BACE1 -/- mice who are also homozygous for an amyloid precursor protein transgene lack brain beta-amyloid and beta-secretase-cleaved APP C-terminal fragments. (33). Brain and primary cortical cultures from BACE1 knockout mice showed no detectable beta-secretase activity, and primary cortical cultures from BACE knockout mice produced much less amyloid-beta from APP. This suggests that BACE1, rather than its paralogue BACE2, is the main beta-secretase for APP.

BACE1 is a protein of 501 amino acids containing a 21-aa signal peptide followed by a proprotein domain spanning aa 22 to 45. There are alternatively spliced forms, BACE-I-457 and BACE-I-476. The lumenal domain of the mature protein is followed by one predicted transmembrane domain and a short cytosolic C-terminal tail of 24 aa. BACE1 is predicted to be a type 1 transmembrane protein with the active site on the

lumenal side of the membrane, where beta-secretase cleaves APP and possible other yet unidentified substrates. BACE1 mRNA in rat brain is present at higher levels in neurons than in glia, supporting that neurons are the primary source of the extracellular A-beta deposited in plaques. Sequence and mass spectrometry analyses showed that asn153, asn172, asn223, and asn354 of the BACE1 ectodomain are N-glycosylation sites. In addition, the ectodomain contains 6 cys residues that form disulfide bridges between positions 216 and 420, 278 and 443, and 330 and 380. The C-terminal domain of BACE1 contains a dileucine motif (LL499/500) that can potentially regulate its trafficking and endocytosis, and an adjacent serine, which is a casein kinase 1 phosphorylation site (S498) (34). The propeptide is predominantly cleaved from BACE1 by furin (35). In cells expressing wit or Swedish mutant APP, transient overexpression of BACE1 decreased alpha-secretase cleavage and increased beta-secretase activity at the known beta-secretase positions, asp1 and glu11. Although BACE1 is clearly a key enzyme required for the processing of APP into Ab, other potential substrates and functions of BACE1 are unknown. Also, no BACE1 interacting proteins with regulatory or modulatory functions have been described. Proteins that activate BACE1 activity would form suitable intervention points for Alzheimer's disease therapy. In addition, proteins that inhibit BACE1, like substrates or pseudosubstrates, could also provide suitable means of intervention e.g. as proteins therapeutics.

APP and the beta-CTF ("C99")

APP is the precursor of Abeta, a peptide which forms the principal component of Alzheimer disease (AD) senile plaques (3) Masters et al. purified the cerebral amyloid protein that forms the plaque core in AD and Down syndrome. Van Nostrand et al. (36) presented evidence that nexin-II, a protease inhibitor that is synthesized and secreted by extravascular cells, is identical to APP. Multhaup et al. (37) demonstrated that APP is involved in copper reduction. They postulated that copper-mediated toxicity may contribute to neurodegeneration in AD, possibly by increased production of hydroxyl radicals. Yan et al. (38) reported that the receptor for advanced glycation end products RAGE is a receptor for the a-beta peptide and that expression of this receptor increases in AD. Expression of RAGE is particularly increased in neurons close to deposits of amyloid beta peptide and to neurofibrillary tangles. Kaneko et al. (39) demonstrated that nanomolar concentrations of various synthetic beta amyloids specifically impaired

mitochondrial succinate dehydrogenase, and speculated that one of the primary targets of beta amyloids is the mitochondrial electron transport chain.

Several missense mutations in the APP gene have been identified that result in early-onset AD: the Swedish APP670/671 double mutation; 3 different mutations at codon 717: the London APP717 mutation, V717I, V717F, and V717G; and the Florida APP716 mutation (Reviewed by Bertram and Tanzi (40)). Most of these AD-related mutations involve amino acid changes near the beta- and gamma-secretase cleavage sites. Two-other missense mutations in the APP gene are located within A-beta near the alpha-secretase cleavage site: the Flemish APP692 mutation, which is associated with cerebral hemorrhage due to congophilic amyloid angiopathy or with early-onset AD with onset age in the mid-forties; and the Dutch APP693 mutation. Almost all AD-linked mutations do elevate secretion of A-beta-42, however, APP693 does not. (41)

Cao and Sudhof (42) demonstrated that the cytoplasmic tail of APP forms a complex with the nuclear adaptor protein Fe65 and the histone acetyltransferase TIP60. This complex stimulates transcription via heterologous Gal4 or LexA DNA binding domains, suggesting that release of the cytoplasmic tail of APP by gamma-cleavage may function in gene expression. The complex could modify expression of genes that function in inflammation (43) or apoptosis (44).

Weggen et al. (45) reported that the nonsteroidal antiinflammatory drugs ibuprofen, indomethacin, and sulindac can decrease the levels of high amyloidogenic amyloid-beta-42 peptide produced from a variety of cultured cells by as much as 80%. This effect was not seen in all NSAIDs and seemed not to be mediated by inhibition of cyclooxygenase (Cox) activity. Weggen et al. (2001) also demonstrated that short-term administration of ibuprofen to mice that produce APP lowered their brain levels of amyloid-beta-42. In cultured cells, the decrease in amyloid-beta-42 secretion was accompanied by an increase in the amyloid-beta(1-38) isoform, indicating that NSAIDs subtly alter gamma-secretase activity without significantly perturbing other APP processing pathways or Notch cleavage.

Proteins and other factors that that regulate APP processing, and especially those that influence levels of Abeta-42 versus other Abeta species, form important potential targets in AD therapy.

Calsenilin

In a yeast two-hybrid screen with the C-terminus of Presenilin 2, a neuronal EF-hand (calcium-binding) protein was identified and named "calsenilin" (46). It interacted with both Presenilin 1 and Presenilin 2 in cells and regulated the levels of a proteolytic product of Presenilin 2. Calsenilin is identical to KChIP3, a protein which was found in a yeast two-hybrid screen for proteins interacting with A-type potassium channels (Kv4.3) (47). KChIP3 i) increased the density of Kv4.2 currents indicating a stabilisation of the channels at the plasma membrane; ii) shifted the current to hyperpolarized potentials; iii) slowed down the kinetics of inactivation and increased the kinetics of recovery.

Calsenilin is also identical to the transcriptional repressor DREAM which acts constitutively to suppress prodynorphin expression in spinal cord neurons (48). Knocking out DREAM results in sufficient dynorphin expression to produce a strong reduction in generalized pain behavior, highlighting the role that intracellular molecules play in modulating pain gating in the spinal cord. Hence proteins that modulate Calsenilin/DREAM activity are interesting targets in nociception.

<u>Tau</u>

Neurofibrillary tangles (NFT), intraneuronal tau protein deposits, are hallmarks of several neurodegenerative disorders such as Alzheimer's and Pick's disease, frontotemporal dementia, cortico-basal degeneration and progressive supranuclear palsy.

The seven tau isoforms are all products of a single gene. Alternative splicing gives rise to six mRNA species differentially expressed in the CNS, depending on stage of neuronal maturation and neuron type. Tau is found mainly in the axon whereas a related protein, MAP2, is mainly found in dendrites.

Tau and MAP2 are microtubule-associated proteins (MAPs) which coassemble with microtubules and colocalise with microtubules in cells. Tau is a nonstructured molecule with a microtubule binding site containing 3 or 4 characteristic amino acid repeat in its carboxyl-terminal half. Alonso et al. (49) noted that in the brains of AD patients the neuronal cytoskeleton is progressively disrupted and replaced by tangles of paired helical filaments (PHFs), and that PHFs are composed mainly of hyperphosphorylated forms of tau. They demonstrated that in solution normal tau associated with the hyperphosphorylated AD P-tau to form large tangles of filaments. They also demonstrated that dephosphorylation with alkaline phosphatase abolished the ability of

AD P-tau to aggregate in vitro. In a form of autosomal dominant inherited dementia known as FTDP17 or Pick disease, the tau gene carries missense mutations or mutations in the 5'- splice site of exon 10, which results in increased levels of tau isoforms with 4 microtubule-binding repeats. These mutations lead to tau molecules that show reduced affinity for microtubules or are more prone to self aggregation.

Proteins and other factors that influence the affinity of tau protein for microtubules, and moreover, influence the aggregation of tau, which is probably mediated by phosphorylation and dephosphorylation events, are important potential targets in AD therapy.

Fe65

Fe65 is a PTB domain- and WW domain-containing adaptor protein that is part of protein complexes at the plasma membrane as well as in the nucleus: It interacts with the Alzheimer's disease amyloid precursor protein (APP; (50)) and related proteins APLP1 and APLP2 (51). Binding of Fe65 to the cytoplasmic tail of APP enhances production of amyloid-forming Abeta peptides (52), but the molecular mechanism of this amyloidogenic effect of Fe65 has not been elucidated. Furthermore, Fe65 stabilizes APP intracellular domain (AICD) (APP intracellular domain (AICD)), the cytosolic product of APP cleavage by gamma-secretase, (53) and forms a nuclear protein complex with TIP60 (42). Little is known about the functional consequences of Fe65-dependent transactivation. The important role of TIP60 in interleukin-1beta- and NF-KappaB-dependent transactivation (43) suggests, however, that the Fe65 complex might function in inflammation.

Fe65 has been shown to bind to the transcription factor CP2/LSF/LBP1 (54) and the low-density lipoprotein receptor-related protein (55), but the significance of these interactions is unknown. Finally, Fe65 has been observed to block cell cycle progression by downregulating thymidylate synthase expression via an unknown mechanism (56).

Understanding the composition of the Fe65 complex, the relationship between its component parts and its regulation might therefore be important in the design of drugs for use in Alzheimer's disease patients as well as for the treatment of various inflammatory conditions and cancer.

X11beta

X11beta/Mint-2 is a neuronal adaptor protein that is believed to be involved in signal transduction processes. It is also regarded as a putative vesicular trafficking protein in the brain that can form a complex with the potential to couple synaptic vesicle exocytosis to neuronal cell adhesion (57).

X11beta interacts with the Alzheimer's disease amyloid precursor protein (APP) (50). Acting synergistically with Munc18a (58), X11beta stabilises APP and inhibits production of proteolytic APP fragments including the A beta peptide that is deposited in the brains of Alzheimer's disease patients (59).

Via a mechanism that depends on its PDZ domain (yet has otherwise not been characterized), X11beta potently inhibits transactivation by an APP-Gal4/VP16 fusion protein (58). Besides interacting with APP, X11beta binds to the C-terminus of presenilin1, although not as strongly as does X11alpha (58). In addition, X11beta has been reported to interact with XB51 (60), but the functional significance of this interaction is unknown.

In Drosophila, dX11beta overexpression in eye imaginal disks causes disruption of compound eye morphology due to enhanced apoptosis of neuronal cells (61). X11beta has been shown to bind to NF-KappaB-p65 through its PDZ domain. This interaction has been implicated in NF-KappaB-dependent Abeta 1-42 production (62).

Elucidation of X11beta complex composition and regulation might therefore help develop novel ways of therapeutic intervention in Alzheimer's disease and inflammation.

3. SUMMARY OF THE INVENTION

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Said object is further achieved by the characterization of component proteins. These proteins are listed in table 2.

Thus, the invention relates to the following embodiments:

- 1. A protein complex selected from complex (I) and comprising (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof. or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active

derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

- 3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions; wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl

(pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the provisio that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

- 5. The complex of any of No. 1 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first ——protein-or-said-second-protein-fused-to-an-amino-acid-sequence-different from the first protein or second protein.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in at least one biochemical activity as stated in table 3.
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps: expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.

- 12. Component of a protein complex obtainable by a process according to any of No. 9 -
- 13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
 - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.
- 16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according

- to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof—which binds to any of the proteins of the group of proteins according to No. 13.
- 18. A kit comprising in one or more containers:
 - (a) the complex of any of No. 1 8 and/or the proteins of No. 13 and/or
 - (b) an antibody according to No. 17 and/or
 - (c) a nucleic acid encoding a protein of the complex of any of No. 1 8 and/or a protein of No. 13 and/or
 - (d) cells expressing the complex of any of No. 1-8 and/or a protein of No. 13 and, optionally,
 - (e) further components such as reagents, buffers and working instructions.
- 19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 8.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 21. Array, preferably a microarray, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for modifying a substrate of a complex of any one of No. 1 8 comprising the step of bringing into contact a complex of any of No. 1 8 with said substrate, such that said substrate is modified.

- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or a protein according to No. 13.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 25. A method for screening for a molecule that binds to a complex of any one of No. 1 8 and/or a protein of No. 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.

- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.
- 41. The complex of any one of No. 1 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of No. 1 ~ 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

3.1 DEFINITIONS

The term "activity" as used herein, refers to the function of a molecule in its broadest sense. It generally includes, but is not limited to, biological, biochemical, physical or chemical functions of the molecule. It includes for example the enzymatic activity, the ability to interact with other molecules and ability to activate, facilitate, stabilize, inhibit, suppress or destabilize the function of other molecules, stability, ability to localize to certain subcellular locations. Where applicable, said term also relates to the function of a protein complex in its broadest sense.

The term "agonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, increases the amount of, or prolongs the duration of, the activity of the complex. The stimulation may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex,

or by a competitive or non-competitive mechanism. Agonists may include proteins, nucleic acids, carbohydrates or any other organic or anorganic molecule or metals. Agonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred activators are those which, when added to the complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 25%, at least 50%, at least 100%, at least, 200%, at least 500% or at least 1000% at a concentration of the activator 1µg ml⁻¹, 10µg ml⁻¹, 100µg ml⁻¹, 500µg ml⁻¹, 1mg ml⁻¹, 10mg ml⁻¹ or 100mg ml⁻¹. Any combination of the above mentioned degrees of percentages and concentration may be used to define an agonist of the invention, with greater effect at lower concentrations being preferred.

The term "amount" as used herein and as applicable to the embodiment described relates to the amount of the particular protein or protein complex described, including the value of null, i.e. where no protein or protein complex described in that particular embodiment is present under the or any of the conditions which might be specified in that particular embodiment.

The term "animal" as used herein includes, but is not limited to mammals, preferably mammals such as cows, pigs, horses, mice, rats, cats, dogs, sheep, goats and most preferably humans. Other animals used in agriculture, such as chickens, ducks etc. are also included in the definition as used herein.

The term "animal" as used herein does not include humans if being used in the context of genetic alterations to the germline.

The term "antagonist" as used herein, means a molecule which modulates the formation of a protein complex or which, when bound to a complex or protein of the invention or a molecule in the protein complex, decreases the amount of, or the duration or level of activity of the complex. The effect may be direct or indirect, including effects on the expression of a gene encoding a member of the protein complex, or by a competitive or non-competitive mechanism. Antagonists may include proteins, including antibodies, nucleic acids, carbohydrates or any other organic or anorganic molecule or metals. Antagonists also include a functional peptide or peptide fragment derived from a protein member of the complexes of the invention or a protein member itself of the complexes of the invention. Preferred antagonists are those which, when added to the

complex and/or the protein of the invention under physiological conditions and/or in vitro assays, including diagnostic or prognostic assays, result in a change of the level of any of the activities of the protein-complex and/or the proteins of the invention as exemplary illustrated above by at least 10%, at least 20%, at least 30%, at least 40% at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 99% at a concentration of the inhibitor of 1µg ml⁻¹, 10µg ml⁻¹, 100µg ml⁻¹, 500µg ml⁻¹, 1mg ml⁻¹, 10mg ml⁻¹ or 100mg ml⁻¹.

Any-combination-of-the-above mentioned degrees of percentages and concentration may be used to define antagonist of the invention, with greater effect at lower concentrations being preferred.

The term "antibodies" as used herein, include include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library.

The term "binding" as used herein means a stable or transient association between two molecules, including electrostatic, hydrophobic, ionic and/or hydrogen-bond interaction under physiological conditions and/or conditions being used in diagnostic or prognostic method or process or procedure.

The term "carrier" as used herein refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

if not stated otherwise, the terms "complex" and "protein complex" are used interchangeably herein and refer to a complex of proteins that is able to perform one or more functions of the wild type protein complex. The protein complex may or may not include and/or be associated with other molecules such as nucleic acid, such as RNA or DNA, or lipids or further cofactors or moleties selected from a metal ions, hormones, second messengers, phosphate, sugars.

A "complex" of the invention may also be part of or a unit of a larger physiological protein assembly.

The term "component of the APP processing pathway" as used herein refers to a protein and/or protein complex which is involved in mediating APP processing in a cell. Components of the APP processing pathway include the following protein complexes as provided herein and components thereof:

Aph1a-complex, APP-695SW-complex, APP-C99-complex, Fe65-complex, Nicastrin-complex, Psen-2-complex, Pen2-complex, Tau-complex, X11ß-complex

If not stated otherwise, the term "compound" as used herein are include but are not limited to peptides, nucleic acids, carbohydrates, natural product extract librariesorganic molecules, preferentially small organic molecules, anorganic molecules, including but not limited to chemicals, metals and organometallic molecules.

The terms "derivatives" or "analogs of component proteins" or "variants" as used herein include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions. It means a protein which is the outcome of a modification of the naturally occurring protein, by amino acid substitutions, deletions and additios, respectively, which derivatives still exhibit the biological function of the

naturally occurring protein although not necessarily to the same degree. The biological function of such proteins can e.g. be examined by suitable available in vitro assays as provided in the invention.

The term "functionally active" as used herein refers to a polypeptide, namely a fragment or derivative, having structural, regulatory, or biochemical functions of the protein according to the embodiment of which this polypeptide, namely fragment or derivative is related to.

The term "fragment" as used herein refers to a polypeptide of at least 10, 20, 30, 40 or 50 amino acids of the component protein according to the embodiment. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids.

The term "gene" as used herein refers to a nucleic acid comprising an open reading frame encoding a polypeptide of, if not stated otherwise, the present invention, including both exon and optionally intron sequences.

The terms "homologue" or "homologous gene products" as used herein mean a protein in another species, preferably mammals, which performs the same biological function as the a protein component of the complex further described herein. Such homologues are also termed "orthologous gene products". The algorithm for the detection of orthologue gene pairs from humans and mammalians or other species uses the whole genome of these organisms. First, pairwise best hits are retrieved, using a full Smith-Waterman alignment of predicted proteins. To further improve reliability, these pairs are clustered with pairwise best hits involving Drosophila melanogaster and C. elegans proteins. Such analysis is given, e.g., in Nature, 2001, 409:860-921. The homologues of the proteins according to the invention can either be isolated based on the sequence homology of the genes encoding the proteins provided herein to the genes of other species by cloning the respective gene applying conventional technology and expressing the protein from such gene, or by isolating proteins of the other species by isolating the analogous complex according to the methods provided herein or to other suitable methods commonly known in the art.

The term "host cells" or, were applicable, "cells" or "hosts" as used herein is intended to be understood in a broadest sense and include, but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and

specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used. It is understood that this term not only refers to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation of environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

The term "modification" as used herein refers to all modifications of a protein or protein complex of the invention including cleavage and addition or removal of a group.

The term "nuleic acid" as used herein refers to polynucleotides such as deoxyribonucleic acid (DNA), and, where appropriate, ribonucleic acid (RNA). They may also be polynucleotides which include within them synthetic or modified nucleotides. A number of different types of modification to polynucleotides are known in the art. These include methylphosphonate and phosphorothioate backbones, addition of acridine or polylysine chains at the 3' and/or 5' ends of the molecule. For the purposes of the present invention, it is to be understood that the polynucleotides described herein may be modified by any method available in the art. Such modifications may be carried out in order to enhance the in vivo activity or lifespan of polynucleotides of the invention. Polynucleotides according to the invention may be produced recombinantly, synthetically, or by any means available to those of skill in the art. They may also be cloned by standard techniques. The polynucleotides are typically provided in isolated and/or purified form. As applicable to the embodiment being described, they include both single stranded and double-stranded polynucleotides.

The term "percent identity", as used herein, means the number of identical residues as defined by an optimal alignment using the Smith-Waterman algorithm divided by the length of the overlap multiplied by 100. The alignment is performed by the search program (Pearson, 1991, Genomics 11:635-650) with the constraint to align the maximum of both sequences.

The terms "polypeptides" and "proteins" are, where applicable, used interchangeably herein. They may be chemically modified, e.g. post-translationally modified. For example, they may be glycosylated or comprise modified amino acid residues. They may also be modified by the addition of a signal sequence to promote their secretion from a cell where the polypeptide does not naturally contain such a sequence. They may be tagged with a tag. They may be tagged with different labels which may assists in identification of the proteins in a protein complex.

Polypeptides/proteins for use in the invention may be in a substantially isolated form. It will be understood that the polypeptid/protein may be mixed with carriers or diluents which will not interfere with the intended purpose of the polypeptide and still be regarded as substantially isolated. A polypeptide/protein for use in the invention may also be in a substantially purified form, in which case it will generally comprise the polypeptide in a preparation in which more than 50%, e.g. more than 80%, 90%, 95% or 99%, by weight of the polypeptide in the preparation is a polypeptide of the invention.

Target for therapeutic drug" means that the respective protein (target) can bind the active ingredient of a pharmaceutical composition and thereby changes its biological activity in response to the drug binding.

The term "tag" as used herein is meant to be understood in its broadest sense and to include, but is not limited to any suitable enzymatic, fluorescent, or radioactive labels and suitable epitopes, incuding but not limited to HA-tag, Myc-tag, T7, His-tag, FLAG-tag, Calmodulin binding proteins, glutathione-S-transferase, strep-tag, KT3-epitope, EEF-epitopes, green-fluorescent protein and variants thereof.

The term "therapeutics" as used herein, includes, but is not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments); antibodies thereto; nucleic acids encoding the component protein, and analogs or derivatives thereof; component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The term "vector" as used herein means a nucleic acid molecule capable of transporting another nucleic acid sequence to which it has been linked. Preferred vectors are those capable of autonomous replication and/or expression of nueclic acids to which they linked. The terms "plasmid" and "vector" are used interchangeably herein when applicable to the embodiment. However, vectors other than plasmids are also included herein. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

4. DETAILED DESCRIPTION OF THE INVENTION

Overview:

An object of the present invention was to identify protein complexes of the beta-amyloid precursor protein (APP) processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the protein complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said protein complex were identified. The components are listed in table 1.

Sald object is further achieved by the characterisation of component proteins. These proteins are listed in table 2.

The invention thus relates to the following embodiments:

1. A protein complex selected from complex (I) and comprising (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

- 2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under lowstringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
 - 3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions; wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
 - 4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant

being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the provisio that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

- 5. The complex of any of No. 1 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in at least one biochemical activity as stated in table 3.
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps: expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.

- 10. The process according to No. 9 wherein the tagged protein comprises two differenttags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component-of-a-protein-complex-obtainable-by-a process-according to-any of No. 9 11.
- 13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, being selected from the second group of proteins according to No. 1 (b) or
 - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a

homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to No. 1.

- 16. Host cell, containing a vector comprising at least one nucleic acid of No. 14 and /or a construct of No. 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to No. 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No.
 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding domain thereof which binds to any of the proteins of the group of proteins according to No. 13.
- 18. A kit comprising in one or more containers:
 - (a) the complex of any of No. 1 8 and/or the proteins of No. 13 and/or
 - (b) an antibody according to No. 17 and/or
 - (c) a nucleic acid encoding a protein of the complex of any of No. 1 8 and/or a protein of No. 13 and/or
 - (d) cells expressing the complex of any of No. 1 8 and/or a protein of No. 13 and, optionally,
 - (e) further components such as reagents, buffers and working instructions.
- 19. The kit according to No. 18 for processing a substrate of a complex of any one of No. 1 8.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 21. Array, preferably a microarray, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 13 and/or at least one antibody according to No. 17 is attached to a solid carrier.

- 22. A process for modifying a substrate of a complex of any one of No. 1 8 comprising the step of bringing into-contact-a complex of any of No. 1 8 with said substrate, such that said substrate is modified.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or a protein according to No. 13.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 25. A method for screening for a molecule that binds to a complex of any one of No. 1 8 and/or a protein of No. 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of No. 1 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules

indicates that the molecule modulates function, activity, or composition of said complex.

- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex is determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.

- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of No. 26 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
 - 36. The method of No. 35, wherein the amount of said complex is determined.
 - 37. The method of No. 35, wherein the activity of said complex is determined.
 - 38. The method of No. 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
 - 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
 - 40. The method of No. 39, wherein said determining step comprises determining whether any of the proteins according to No. 13 is present in the complex.

- 41. The complex of any one of No. 1 8, or a protein of No. 13 or an antibody or fragment thereof of No. 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of No. 1 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

Animal models are also provided herein.

Preferably, the protein components of the complexes described herein are all mammalian proteins. The complexes can also consist only of the respective homologues from other mammals such as mouse, rat, pig, cow, dog, monkey, sheep or horse or other species such as D. melanogaster, C. elegans or chicken. In another preferred embodiment, the complexes are a mixture of proteins from two or more species.

TABLES:

Table 1: Composition of Complexes

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Entry point'): Lists the bait proteins that have been chosen for the purification of the given complex.

Third column ('All interactors'): Lists all novel interactors which have been identified as members of the complex and all interactors which have been known to be associated with the bait so far.

Fourth column ('Known interactors'): Lists all interactors which have been known to be associated with the bait so far.

Fifth column ('Novel interactors of the complex'): Lists all novel interactors of the complex which have been identified in the experiments provided herein.

Sixth column: Separately lists the members of the newly identified complex which have not been annotated previously.

Table 2: Individual Proteins of the Complexes

First column ('Protein'): Lists in alphabetical order all proteins which have been identified as interactors of the complexes presented herein.

Second column ('SEQ ID'): Lists the SEQ ID (Sequence Identifications) of the proteins herein as used herein.

Third column ('IPI-Numbers'): Lists the IPI-Numbers of the proteins herein. The IPI-Numbers refer to the International Protein Index created by the European Bioinformatics Institute (EMBL-EBI), Hinxton, UK.

Fourth column ('Molecular Weight'): Lists the Molecular Weight of the proteins in Dalton.

Table 3: Biochemical Activities of the Complexes of the invention.

First column ('Name of complex'): Lists the name of the protein complexes as used herein.

Second column ('Biochemical Activity'): Lists biochemical activities of the complexes. Assays in order to test these activities are also provided herein (infra).

Table 4: Medical Applications of the Complexes of the invention

First column ('Name of complex'): Lists the name of the protein compelxes as used herein

Second column ('Medical application'): lists disorder, diseases, disease areas etc. which are treatable and/or preventable and/or diagnosable etc. by therapeutics and methods interacting with/acting via the complex.

4.1 PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The protein complexes of the present invention and their component proteins are described in the Tables 1 - 4. The protein complexes and component proteins can be obtained by methods well known in the art for protein purification and recombinant protein expression. For example, the protein complexes of the present invention can be isolated using the TAP method described in Section 5, infra, and in WO 00/09716 and Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032, which are each incorporated by reference in their entirety. Additionally, the protein complexes can be isolated by immunoprecipitation of the component proteins and combining the immunoprecipitated proteins. The protein complexes can also be produced by recombinantly expressing the component proteins and combining the expressed proteins.

The nucleic and amino acid sequences of the component proteins of the protein complexes of the present invention are provided herein (SEQ ID NO 1 - 315), and can be obtained by any method known in the art, e.g., by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of each sequence, and/or by cloning from a cDNA or genomic library using an oligonucleotide specific for each nucleotide sequence.

Homologues (e.g., nucleic acids encoding component proteins from other species) or other related sequences (e.g., variants, paralogs) which are members of a native cellular protein complex can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular nucleic acid sequence as a probe, using methods well known in the art for nucleic acid hybridization and cloning.

Exemplary moderately stringent hybridization conditions are as follows: prehybridization of filters containing DNA is carried out for 8 hours to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 μ g/ml denatured salmon sperm DNA. Filters are hybridized for 48 hours at 65°C in prehybridization mixture containing 100 μ g/ml denatured salmon sperm DNA and 5-20 X 10⁶ cpm of ³²P-labeled probe. Washing of filters is done at 37°C

for 1 hour in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 °C for 45 min before autoradiography. Alternatively, exemplary conditions of high stringency are as follows: e.g., hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1xSSC/0.1% SDS at 68°C (Ausubel et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Other conditions of high stringency which may be used—are—well known—in—the—art.—Exemplary low stringency hybridization conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 μg/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

For recombinant expression of one or more of the proteins, the nucleic acid containing all or a portion of the nucleotide sequence encoding the protein can be inserted into an appropriate expression vector, i.e., a vector that contains the necessary elements for the transcription and translation of the inserted protein coding sequence. The necessary transcriptional and translational signals can also be supplied by the native promoter of the component protein gene, and/or flanking regions.

A variety of host-vector systems may be utilized to express the protein coding sequence. These include but are not limited to mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); microorganisms such as yeast containing yeast vectors; or bacteria transformed with bacteriophage, DNA, plasmid DNA, or cosmid DNA. The expression elements of vectors vary in their strengths and specificities. Depending on the host-vector system utilized, any one of a number of suitable transcription and translation elements may be used.

In a preferred embodiment, a complex of the present invention is obtained by expressing the entire coding sequences of the component proteins in the same cell, either under the control of the same promoter or separate promoters. In yet another embodiment, a derivative, fragment or homologue of a component protein is recombinantly expressed. Preferably the derivative, fragment or homologue of the protein forms a complex with the other components of the complex, and more preferably

forms a complex that binds to an anti-complex antibody. Such an antibody is further described infra.

Any method available in the art can be used for the insertion of DNA fragments into a vector to construct expression vectors containing a chimeric gene consisting of appropriate transcriptional/translational control signals and protein coding sequences. These methods may include in vitro recombinant DNA and synthetic techniques and in vivo recombinant techniques (genetic recombination). Expression of nucleic acid sequences encoding a component protein, or a derivative, fragment or homologue thereof, may be regulated by a second nucleic acid sequence so that the gene or fragment thereof is expressed in a host transformed with the recombinant DNA molecule(s). For example, expression of the proteins may be controlled by any promoter/enhancer known in the art. In a specific embodiment, the promoter is not native to the gene for the component protein. Promoters that may be used can be selected from among the many known in the art, and are chosen so as to be operative in the selected host cell.

In a specific embodiment, a vector is used that comprises a promoter operably linked to nucleic acid sequences encoding a component protein, or a fragment, derivative or homologue thereof, one or more origins of replication, and optionally, one or more selectable markers (e.g., an antibiotic resistance gene).

In another specific embodiment, an expression vector containing the coding sequence, or a portion thereof, of a component protein, either together or separately, is made by subcloning the gene sequences into the EcoRI restriction site of each of the three pGEX vectors (glutathione S-transferase expression vectors; Smith and Johnson, 1988, Gene 7:31-40). This allows for the expression of products in the correct reading frame.

Expression vectors containing the sequences of interest can be identified by three general approaches: (a) nucleic acid hybridization, (b) presence or absence of "marker" gene function, and (c) expression of the inserted sequences. In the first approach, coding sequences can be detected by nucleic acid hybridization to probes comprising sequences homologous and complementary to the inserted sequences. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "marker" functions (e.g., resistance to antibiotics, occlusion body formation in baculovirus, etc.) caused by insertion of the sequences of interest in the vector. For example, if a component protein gene, or portion

thereof, is inserted within the marker gene sequence of the vector, recombinants containing the encoded protein or portion will be identified by the absence of the marker gene function (e.g., loss of β-galactosidase activity). In the third approach, recombinant expression vectors can be identified by assaying for the component protein expressed by the recombinant vector. Such assays can be based, for example, on the physical or functional properties of the interacting species in in vitro assay systems, e.g., formation of a complex comprising the protein or binding to an anti-complex antibody.

or individual proteins isolated, several methods known in the art can be used to propagate them. Using a suitable host system and growth conditions, recombinant expression vectors can be propagated and amplified in quantity. As previously described, the expression vectors or derivatives which can be used include, but are not limited to, human or animal viruses such as vaccinia virus or adenovirus; insect viruses such as baculovirus, yeast vectors; bacteriophage vectors such as lambda phage; and plasmid and cosmid vectors.

In addition, a host cell strain may be chosen that modulates the expression of the inserted sequences, or modifies or processes the expressed proteins in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically-engineered component proteins may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (e.g., glycosylation, phosphorylation, etc.) of proteins. Appropriate cell lines or host systems can be chosen to ensure that the desired modification and processing of the foreign protein is achieved. For example, expression in a bacterial system can be used to produce an unglycosylated core protein, while expression in mammalian cells ensures "native" glycosylation of a heterologous protein. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

In other specific embodiments, a component protein or a fragment, homologue or derivative thereof, may be expressed as fusion or chimeric protein product comprising the protein, fragment, homologue, or derivative joined via a peptide bond to a heterologous protein sequence of a different protein. Such chimeric products can be made by ligating the appropriate nucleic acid sequences encoding the desired amino acids to each other by methods known in the art, in the proper coding frame, and expressing the chimeric products in a suitable host by methods commonly known in the

art. Alternatively, such a chimeric product can be made by protein synthetic techniques, e.g., by use of a peptide synthesizer. Chimeric genes comprising a portion of a component protein fused to any heterologous protein-encoding sequences may be constructed.

In particular, protein component derivatives can be made by altering their sequences by substitutions, additions or deletions that provide for functionally equivalent Due to the degeneracy of nucleotide coding sequences, other DNA sequences that encode substantially the same amino acid sequence as a component gene or cDNA can be used in the practice of the present invention. These include but are not limited to nucleotide sequences comprising all or portions of the component protein gene that are altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change. Likewise, the derivatives of the invention include, but are not limited to, those containing, as a primary amino acid sequence, all or part of the amino acid sequence of a component protein, including altered sequences in which functionally equivalent amino acid residues are substituted for residues within the sequence resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity that acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

In a specific embodiment, up to 1%, 2%, 5%, 10%, 15% or 20% of the total number of amino acids in the wild type protein are substituted or deleted; or 1, 2, 3, 4, 5, or 6 or up to 10 or up to 20 amino acids are inserted, substituted or deleted relative to the wild type protein.

In a specific embodiment of the invention, the nucleic acids encoding a protein component and protein components consisting of or comprising a fragment of or consisting of at least 6 (continuous) amino acids of the protein are provided. In other embodiments, the fragment consists of at least 10, 20, 30, 40, or 50 amino acids of the

component protein. In specific embodiments, such fragments are not larger than 35, 100 or 200 amino acids. Derivatives or analogs of component proteins include, but are not limited, to molecules comprising regions that are substantially homologous to the component proteins, in various embodiments, by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to a sequence encoding the component protein under stringent, moderately stringent, or nonstringent conditions.

In a specific embodiment, proteins are provided herein, which share an identical region of 20, 30, 40, 50 or 60 contiguous amino acids of the proteins listed in table 2.

The protein component derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations which result in their production can occur at the gene or protein level. For example, the cloned gene sequences can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The sequences can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated in vitro. In the production of the gene encoding a derivative, homologue or analog of a component protein, care should be taken to ensure that the modified gene retains the original translational reading frame, uninterrupted by translational stop signals, in the gene region where the desired activity is encoded.

Additionally, the encoding nucleic acid sequence can be mutated in vitro or in vivo, to create and/or destroy translation, initiation, and/or termination sequences, or to create variations in coding regions and/or form new restriction endonuclease sites or destroy pre-existing ones, to facilitate further in vitro modification. Any technique for mutagenesis known in the art can be used, including but not limited to, chemical mutagenesis and in vitro site-directed mutagenesis (Hutchinson et al., 1978, J. Biol. Chem. 253:6551-6558), amplification with PCR primers containing a mutation, etc.

Once a recombinant cell expressing a component protein, or fragment or derivative thereof, is identified, the individual gene product or complex can be isolated and analyzed. This is achieved by assays based on the physical and/or functional properties of the protein or complex, including, but not limited to, radioactive labeling of

the product followed by analysis by gel electrophoresis, immunoassay, cross-linking to marker-labeled product, etc.

The component proteins and complexes may be isolated and purified by standard methods known in the art (either from natural sources or recombinant host cells expressing the complexes or proteins), including but not restricted to column chromatography (e.g., ion exchange, affinity, gel exclusion, reversed-phase high pressure, fast protein liquid, etc.), differential centrifugation, differential solubility, or by any other standard technique used for the purification of proteins. Functional properties may be evaluated using any suitable assay known in the art.

Alternatively, once a component protein or its derivative, is identified, the amino acid sequence of the protein can be deduced from the nucleic acid sequence of the chimeric gene from which it was encoded. As a result, the protein or its derivative can be synthesized by standard chemical methods known in the art (e.g., Hunkapiller et al., 1984, Nature 310:105-111).

Manipulations of component protein sequences may be made at the protein level. Included within the scope of the invention is a complex in which the component proteins or derivatives and analogs that are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄, acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

In specific embodiments, the amino acid sequences are modified to include a fluorescent label. In another specific embodiment, the protein sequences are modified to have a heterofunctional reagent; such heterofunctional reagents can be used to crosslink the members of the complex.

In addition, complexes of analogs and derivatives of component proteins can be chemically synthesized. For example, a peptide corresponding to a portion of a component protein, which comprises the desired domain or mediates the desired activity in vitro (e.g., complex formation) can be synthesized by use of a peptide synthesizer. Furthermore, if desired, non-classical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the protein sequence.

In cases where natural products are suspected of being mutant or are isolated from new species, the amino acid sequence of a component protein isolated from the natural source, as well as those expressed in vitro, or from synthesized expression vectors in vivo or in vitro, can be determined from analysis of the DNA sequence, or alternatively, by direct sequencing of the isolated protein. Such analysis can be performed by manual sequencing or through use of an automated amino acid sequenator.

The complexes can also be analyzed by hydrophilicity analysis (Hopp and Woods, 1981, Proc. Natl. Acad. Sci. USA 78:3824-3828). A hydrophilicity profile can be used to identify the hydrophobic and hydrophilic regions of the proteins, and help predict their orientation in designing substrates for experimental manipulation, such as in binding experiments, antibody synthesis, etc. Secondary structural analysis can also be done to identify regions of the component proteins, or their derivatives, that assume specific structures (Chou and Fasman, 1974, Biochemistry 13:222-23). Manipulation, translation, secondary structure prediction, hydrophilicity and hydrophobicity profile predictions, open reading frame prediction and plotting, and determination of sequence homologies, etc., can be accomplished using computer software programs available in the art.

Other methods of structural analysis including but not limited to X-ray crystallography (Engstrom, 1974, Biochem. Exp. Biol. 11:7-13), mass spectroscopy and gas chromatography (Methods in Protein Science, J. Wiley and Sons, New York, 1997), and computer modeling (Fletterick and Zoller, eds., 1986, Computer Graphics and Molecular Modeling, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, New York) can also be employed.

4.2 ANTIBODIES TO PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

According to the present invention, a protein complex of the present invention comprising a first protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, selected from the group consisting of proteins listed in fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, can be used as an immunogen to generate antibodies which immunospecifically bind such

immunogen. According to the present invention, also a protein complex of the present invention can be used as an immunogen to generate antibodies which immunospecifically bind to such immunogen comprising all proteins listed in fifth column of table 1.

Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and an Fab expression library. In a specific embodiment, antibodies to a complex comprising human protein components are produced. In another embodiment, a complex formed from a fragment of said first protein and a fragment of said second protein, which fragments contain the protein domain that interacts with the other member of the complex, are used as an immunogen for antibody production. In a preferred embodiment, the antibody specific for the complex in that the antibody does not bind the individual protein components of the complex.

Polyclonal antibodies can be prepared as described above by immunizing a suitable subject with a polypeptide of the invention as an immunogen. Preferred polyclonal antibody compositions are ones that have been selected for antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred polyclonal antibody preparations are ones that contain only antibodies directed against a polypeptide or polypeptides of the invention. Particularly preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a polypeptide of the invention. In such a manner, the only human epitope or epitopes recognized by the resulting antibody compositions raised against this immunogen will be present as part of a polypeptide or polypeptides of the invention.

The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide. If desired, the antibody molecules can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. Alternatively, antibodies specific for a protein or polypeptide of the invention can be selected for (e.g., partially purified) or purified by, e.g., affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies

specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, i.e., one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those on the desired protein or polypeptide of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most-5% (by-dry-weight)-of-the-sample is-contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein or polypeptide of the invention.

At an appropriate time after immunization, e.g., when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein, 1975, Nature 256:495-497, the human B cell hybridoma technique (Kozbor et al., 1983, Immunol. Today 4:72), the EBV-hybridoma technique (Cole et al., 1985, Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally Current Protocols in Immunology 1994, Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a polypeptide of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/01049; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al.,

1991, Bio/Technology 9:1370-1372; Hay et al., 1992, Hum. Antibod. Hybridomas 3:81-85; Huse et al., 1989, Science 246:1275-1281; Griffiths et al., 1993, EMBO J. 12:725-734.

Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from nonhuman species having one or more complementarily determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al., 1988, Science 240:1041-1043; Liu et al., 1987, Proc. Natl. Acad. Sci. USA 84:3439-3443; Liu et al., 1987, J. Immunol. 139:3521-3526; Sun et al., 1987, Proc. Natl. Acad. Sci. USA 84:214-218; Nishimura et al., 1987, Canc. Res. 47:999-1005; Wood et al., 1985, Nature 314:446-449; and Shaw et al., 1988, J. Natl. Cancer Inst. 80:1553-1559); Morrison, 1985, Science 229:1202-1207; Oi et al., 1986, Bio/Techniques 4:214; U.S. Patent 5,225,539; Jones et al., 1986, Nature 321:552-525; Verhoeyan et al., 1988, Science 239:1534; and Beidler et al., 1988, J. Immunol. 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell

differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, 1995, Int. Rev. Immunol. 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., 1994, Bio/technology 12:899-903).

Antibody fragments that contain the idiotypes of the complex can be generated by techniques known in the art. For example, such fragments include, but are not limited to, the F(ab')2 fragment which can be produced by pepsin digestion of the antibody molecule; the Fab' fragment that can be generated by reducing the disulfide bridges of the F(ab')2 fragment; the Fab fragment that can be generated by treating the antibody molecular with papain and a reducing agent; and Fv fragments.

In the production of antibodies, screening for the desired antibody can be accomplished by techniques known in the art, e.g., ELISA (enzyme-linked immunosorbent assay). To select antibodies specific to a particular domain of the complex, or a derivative thereof, one may assay generated hybridomas for a product that binds to the fragment of the complex, or a derivative thereof, that contains such a domain. For selection of an antibody that specifically binds a complex of the present, or a derivative, or homologue thereof, but which does not specifically bind to the individual proteins of the complex, or a derivative, or homologue thereof, one can select on the basis of positive binding to the complex and a lack of binding to the individual protein components.

Antibodies specific to a domain of the complex, or a derivative, or homologue thereof, are also provided.

The foregoing antibodies can be used in methods known in the art relating to the localization and/or quantification of the complexes of the invention, e.g., for imaging these proteins, measuring levels thereof in appropriate physiological samples (by immunoassay), in diagnostic methods, etc. This hold true also for a derivative, or homologue thereof of a complex.

In another embodiment of the invention (see infra), an antibody to a complex or a fragment of such antibodies containing the antibody binding domain, is a therapeutic.

4.3 <u>DIAGNOSTIC</u>, <u>PROGNOSTIC</u>, <u>AND SCREENING USES OF THE PROTEIN COMPLEXES/PROTEINS OF THE INVENTION</u>

The particular protein complexes and proteins of the present invention may be markers of normal physiological processes, and thus have diagnostic utility. Further, definition of particular groups of patients with elevations or deficiencies of a protein complex of the present invention, or wherein the protein complex has a change in protein component composition, can lead to new nosological classifications of diseases, furthering diagnostic ability.

Examples for diseases or disorders are those as listed in table 4

Detecting levels of protein complexes, or individual component proteins that form the complexes, or detecting levels of the mRNAs encoding the components of the complex, may be used in diagnosis, prognosis, and/or staging to follow the course of a disease state, to follow a therapeutic response, etc.

A protein complex of the present invention and the individual components of the complex and a derivative, analog or subsequence thereof, encoding nucleic acids (and sequences complementary thereto), and anti-complex antibodies and antibodies directed against individual components that can form the complex, are useful in diagnostics. The foregoing molecules can be used in assays, such as immunoassays, to detect, prognose, diagnose, or monitor various conditions, diseases, and disorders characterized by aberrant levels of a complex or aberrant component composition of a complex, or monitor the treatment of such various conditions, diseases, and disorders.

In particular, such an immunoassay is carried out by a method comprising contacting a sample derived from a patient with an anti-complex antibody under conditions such that immunospecific binding can occur, and detecting or measuring the

amount of any immunospecific binding by the antibody. In a specific aspect, such binding of antibody, in tissue sections, can be used to detect aberrant complex localization, or aberrant (e.g., high, low or absent) levels of a protein complex or complexes. In a specific embodiment, an antibody to the complex can be used to assay a patient tissue or serum sample for the presence of the complex, where an aberrant level of the complex is an indication of a diseased condition. By "aberrant levels" is meant increased or decreased levels relative to that present, or a standard level representing that present, in an analogous sample from a portion or fluid of the body, or from a subject not having the disorder.

The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as Western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few known in the art.

Nucleic acids encoding the components of the protein complex and related nucleic acid sequences and subsequences, including complementary sequences, can be used in hybridization assays. The nucleic acid sequences, or subsequences thereof, comprising about at least 8 nucleotides, can be used as hybridization probes. Hybridization assays can be used to detect, prognose, diagnose, or monitor conditions, disorders, or disease states associated with aberrant levels of the mRNAs encoding the components of a complex as described, supra. In particular, such a hybridization assay is carried out by a method comprising contacting a sample containing nucleic acid with a nucleic acid probe capable of hybridizing to component protein coding DNA or RNA, under conditions such that hybridization can occur, and detecting or measuring any resulting hybridization.

In specific embodiments, diseases and disorders involving or characterized by aberrant levels of a protein complex or aberrant complex composition can be diagnosed, or its suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by determining the component protein composition of the complex, or detecting aberrant levels of a member of the complex or un-complexed component proteins or encoding nucleic acids, or functional activity including, but not restricted to, binding to an interacting partner, or by detecting mutations in component

protein RNA, DNA or protein (e.g., mutations such as translocations, truncations, changes in nucleotide or amino acid sequence relative to wild-type that cause increased or decreased expression or activity of a complex, and/or component protein.

Such diseases and disorders include, but are not limited to neurodegenerative disease such as listed in table 4.

By way of example, levels of a protein complex and the individual components of a complex can be detected by immunoassay, levels of component protein RNA or DNA can be detected by hybridization assays (e.g., Northern blots, dot blots, RNase protection assays), and binding of component proteins to each other (e.g., complex formation) can be measured by binding assays commonly known in the art. Translocations and point mutations in component protein genes can be detected by Southern blotting, RFLP analysis, PCR using primers that preferably generate a fragment spanning at least most of the gene by sequencing of genomic DNA or cDNA obtained from the patient, etc.

Assays well known in the art (e.g., assays described above such as immunoassays, nucleic acid hybridization assays, activity assays, etc.) can be used to determine whether one or more particular protein complexes are present at either increased or decreased levels, or are absent, in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the levels in samples from subjects not having such a disease or disorder, or having a predisposition to develop such a disease or disorder. Additionally, these assays can be used to determine whether the ratio of the complex to the un-complexed components of the complex, is increased or decreased in samples from patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, as compared to the ratio in samples from subjects not having such a disease or disorder.

In the event that levels of one or more particular protein complexes (i.e., complexes formed from component protein derivatives, homologs, fragments, or analogs) are determined to be increased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder, or predisposition for a disease or disorder, can be diagnosed, have prognosis defined for, be screened for, or be monitored by detecting increased levels of the one or more protein complexes, increased levels of the mRNA

that encodes one or more members of the one or more particular protein complexes, or by detecting increased complex functional activity.

Accordingly, in a specific embodiment of the present invention, diseases and disorders involving increased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting increased levels of the one or more protein complexes, the mRNA encoding both members of the complex, or complex functional activity, or by detecting mutations in the component proteins that stabilize or enhance complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that stabilize or enhance complex formation.

In the event that levels of one or more particular protein complexes are determined to be decreased in patients suffering from a particular disease or disorder, or having a predisposition to develop such a disease or disorder, then the particular disease or disorder or predisposition for a disease or disorder can be diagnosed, have its prognosis determined, be screened for, or be monitored by detecting decreased levels of the one or more protein complexes, the mRNA that encodes one or more members of the particular one or more protein complexes, or by detecting decreased protein complex functional activity.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving decreased levels of one or more protein complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting decreased levels of the one or more protein complexes, the mRNA encoding one or more members of the one or more complexes, or complex functional activity, or by detecting mutations in the component proteins that decrease complex formation, e.g., mutations such as translocations in nucleic acids, truncations in the gene or protein, changes in nucleotide or amino acid sequence relative to wild-type, that decrease complex formation.

Accordingly, in a specific embodiment of the invention, diseases and disorders involving aberrant compositions of the complexes can be diagnosed, or their suspected presence can be screened for, or a predisposition to develop such disorders can be detected, by detecting the component proteins of one or more complexes, or the mRNA encoding the members of the one or more complexes.

The use of detection techniques, especially those involving antibodies against a protein complex, provides a method of detecting specific cells that express the complex or component proteins. Using such assays, specific cell types can be defined in which one or more particular protein complexes are expressed, and the presence of the complex or component proteins can be correlated with cell viability, state, health, etc.

Also embodied are methods to detect a protein complex of the present invention in cell culture models that express particular protein complexes or derivatives thereof, for the purpose of characterizing or preparing the complexes for harvest. This embodiment includes cell sorting of prokaryotes such as but not restricted to bacteria (Davey and Kell, 1996, Microbiol. Rev. 60:641-696), primary cultures and tissue specimens from eukaryotes, including mammalian species such as human (Steele et al., 1996, Clin. Obstet. Gynecol 39:801-813), and continuous cell cultures (Orfao and Ruiz-Arguelles, 1996, Clin. Biochem. 29:5-9). Such isolations can be used as methods of diagnosis, described, supra.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an abberant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods-to-study changes in-the-activity-of-proteins-dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

4.4 THERAPEUTIC USES OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION

The present invention is directed to a method for treatment or prevention of various diseases and disorders by administration of a therapeutic compound (termed herein "therapeutic"). Such "therapeutics" include, but are not limited to, a protein complex of the present invention, the individual component proteins, and analogs and derivatives (including fragments) of the foregoing (e.g., as described hereinabove); antibodies thereto (as described hereinabove); nucleic acids encoding the component protein, and analogs or derivatives, thereof (e.g., as described hereinabove); component protein antisense nucleic acids, and agents that modulate complex formation and/or activity (i.e., agonists and antagonists).

The protein complexes as identified herein can be implicated in processes which are implicated in or associated with pathological conditions.

Diseases and disorders which can be treated and/or prevented and/or diagnosed by therapeutics interacting with any of the complexes provided herein are for example those listed in table 4.

These disorders are treated or prevented by administration of a therapeutic that modulates (i.e. inhibits or promotes) protein complex activity or formation or modulates its function or composition. Diseases or disorders associated with aberrant levels of complex activity or formation, or aberrant levels or activity of the component proteins, or aberrant complex composition or a change in the function, may be treated by

administration of a therapeutic that modulates complex formation or activity or by the administration of a protein complex.

Therapeutics may also be administered to modulate complex formation or activity or level thereof in a microbial organism such as yeast, fungi such as candida albicans causing an infectious disease in animals or humans.

Diseases and disorders characterized by increased (relative to a subject not suffering from the disease or disorder) complex levels or activity can be treated with therapeutics that antagonize (i.e., reduce or inhibit) complex formation or activity. Therapeutics that can be used include, but are not limited to, the component proteins or an analog, derivative or fragment of the component protein; anti-complex antibodies (e.g., antibodies specific for the protein complex, or a fragment or derivative of the antibody containing the binding region thereof; nucleic acids encoding the component proteins; antisense nucleic acids complementary to nucleic acids encoding the component proteins; and nucleic acids encoding the component protein that are dysfunctional due to, e.g., a heterologous insertion within the protein coding sequence, that are used to "knockout" endogenous protein function by homologous recombination, see, e.g., Capecchi, 1989, Science 244:1288-1292. In one embodiment, a therapeutic is 1, 2 or more antisense nucleic acids which are complementary to 1, 2, or more nucleic acids, respectfully, that encode component proteins of a complex.

In a specific embodiment of the present invention, a nucleic acid containing a portion of a component protein gene in which gene sequences flank (are both 5' and 3' to) a different gene sequence, is used as a component protein antagonist, or to promote component protein inactivation by homologous recombination (see also, Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342: 435-438). Additionally, mutants or derivatives of a component protein that has greater affinity for another component protein or the complex than wild type may be administered to compete with wild type protein for binding, thereby reducing the levels of complexes containing the wild type protein. Other therapeutics that inhibit complex function can be identified by use of known convenient in vitro assays, e.g., based on their ability to inhibit complex formation, or as described in Section 4.5, infra.

In specific embodiments, therapeutics that antagonize complex formation or activity are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an increased (relative to normal or desired) level of a complex, for example, in patients where complexes are overactive or overexpressed; or (2) in

diseases or disorders where an in vitro (or in vivo) assay (see infra) indicates the utility of antagonist administration. Increased levels of a complex can be readily detected, e.g., by quantifying protein and/or RNA, by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, or structure and/or activity of the expressed complex (or the encoding mRNA). Many methods standard in the art can be thus employed including, but not limited to, immunoassays to detect complexes and/or visualize complexes (e.g., Western blot analysis, immunoprecipitation followed by sodium—dodecyl—sulfate polyacrylamide gel—electrophoresis [SDS-PAGE], immunocytochemistry, etc.), and/or hybridization assays to detect concurrent expression of component protein mRNA (e.g., Northern assays, dot blot analysis, in situ hybridization, etc.).

A more specific embodiment of the present invention is directed to a method of reducing complex expression (i.e., expression of the protein components of the complex and/or formation of the complex) by targeting mRNAs that express the protein moieties. RNA therapeutics currently fall within three classes, antisense species, ribozymes, or RNA aptamers (Good et al., 1997, Gene Therapy 4:45-54).

Antisense oligonucleotides have been the most widely used. By way of example, but not limitation, antisense oligonucleotide methodology to reduce complex formation is presented below, infra. Ribozyme therapy involves the administration, induced expression, etc. of small RNA molecules with enzymatic ability to cleave, bind, or otherwise inactivate specific RNAs, to reduce or eliminate expression of particular proteins (Grassi and Marini, 1996, Annals of Medicine 28:499-510; Gibson, 1996, Cancer and Metastasis Reviews 15:287-299). RNA aptamers are specific RNA ligand proteins, such as for Tat and Rev RNA (Good et al., 1997, Gene Therapy 4:45-54) that can specifically inhibit their translation. Aptamers specific for component proteins can be identified by many methods well known in the art, for example, by affecting the formation of a complex in the protein-protein interaction assay described, infra.

In another embodiment, the activity or levels of a component protein are reduced by administration of another component protein, or the encoding nucleic acid, or an antibody that immunospecifically binds to the component protein, or a fragment or a derivative of the antibody containing the binding domain thereof.

In another aspect of the invention, diseases or disorders associated with increased levels of an component protein of the complex may be treated or prevented by administration of a therapeutic that increases complex formation if the complex formation

acts to reduce or inactivate the component protein through complex formation. Such diseases or disorders can be treated or prevented by administration of one component member of the complex, administration of antibodies or other molecules that stabilize the complex, etc.

Diseases and disorders associated with underexpression of a complex, or a component protein, are treated or prevented by administration of a therapeutic that promotes (i.e., increases or supplies) complex levels and/or function, or individual component protein function. Examples of such a therapeutic include but are not limited to a complex or a derivative, analog or fragment of the complex that are functionally active (e.g., able to form a complex), un-complexed component proteins and derivatives, analogs, and fragments of un-complexed component proteins, and nucleic acids encoding the members of a complex or functionally active derivatives or fragments of the members of the complex, e.g., for use in gene therapy. In a specific embodiment, a therapeutic includes derivatives, homologs or fragments of a component protein that increase and/or stabilize complex formation. Examples of other agonists can be identified using in vitro assays or animal models, examples of which are described, infra.

In yet other specific embodiments of the present invention, therapeutics that promote complex function are administered therapeutically, including prophylactically, (1) in diseases or disorders involving an absence or decreased (relative to normal or desired) level of a complex, for example, in patients where a complex, or the individual components necessary to form the complex, is lacking, genetically defective, biologically inactive or underactive, or under-expressed; or (2) in diseases or disorders wherein an in vitro or in vivo assay (see, infra) indicates the utility of complex agonist administration. The absence or decreased level of a complex, component protein or function can be readily detected, e.g., by obtaining a patient tissue sample (e.g., from biopsy tissue) and assaying it in vitro for RNA or protein levels, structure and/or activity of the expressed complex and/or the concurrent expression of mRNA encoding the two components of the complex. Many methods standard in the art can be thus employed, including but not limited to immunoassays to detect and/or visualize a complex, or the individual components of a complex (e.g., Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs encoding the individual protein components of a complex by detecting and/or visualizing

component mRNA concurrently or separately using, e.g., Northern assays, dot blot analysis, in situ hybridization, etc.

In specific embodiments, the activity or levels of a component protein are increased by administration of another component protein of the same complex, or a derivative, homolog or analog thereof, a nucleic acid encoding the other component, or an agent that stabilizes or enhances the other component, or a fragment or derivative of such an agent.

Generally, administration of products of species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, a human complex, or derivative, homolog or analog thereof; nucleic acids encoding the members of the human complex or a derivative, homolog or analog thereof; an antibody to a human complex, or a derivative thereof; or other human agents that affect component proteins or the complex, are therapeutically or prophylactically administered to a human patient.

Preferably, suitable in vitro or in vivo assays are utilized to determine the effect of a specific therapeutic and whether its administration is indicated for treatment of the affected tissue or individual.

In various specific embodiments, in vitro assays can be carried out with representative cells of cell types involved in a patient's disorder, to determine if a therapeutic has a desired effect upon such cell types.

Compounds for use in therapy can be tested in suitable animal model systems prior to testing in humans, including, but not limited to, rats, mice, chicken, cows, monkeys, rabbits, etc. For in vivo testing, prior to administration to humans, any animal model system known in the art may be used. Additional descriptions and sources of therapeutics that can be used according to the invention are found in Sections 4.1 to 4.3 and 4.7 herein.

4.4.1 GENE THERAPY

In a specific embodiment of the present invention, nucleic acids comprising a sequence encoding the component proteins, or a functional derivative thereof, are administered to modulate complex activity or formation by way of gene therapy. Gene therapy refers to therapy performed by the administration of a nucleic acid to a subject.

In this embodiment of the present invention, the nucleic acid expresses its encoded protein(s) that mediates a therapeutic effect by modulating complex activity or formation. Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, Clinical Pharmacy 12:488-505; Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, 1993, Science 260:926-932; Morgan and Anderson, 1993, Ann. Rev. Biochem. 62;191-217; and May, 1993, TIBTECH 11:155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al., eds., 1993, Current Protocols in Molecular Biology, John Wiley & Sons, NY; and Kriegler, 1990, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY.

In a preferred aspect, the therapeutic comprises a nucleic acid that is part of an expression vector that expresses one or more of the component proteins, or fragments or chimeric proteins thereof, in a suitable host. In particular, such a nucleic acid has a promoter operably linked to the protein coding region(s) (or, less preferably separate promoters linked to the separate coding regions separately), said promoter being inducible or constitutive, and optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule is used in which the coding sequences, and any other desired sequences, are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intra-chromosomal expression of the component protein nucleic acids (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

Delivery of the nucleic acid into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vector, or indirect, in which case, cells are first transformed with the nucleic acid in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid is directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by infection using a defective or attenuated retroviral or other viral vector (U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle

bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors, or through use of transfecting agents, by encapsulation in liposomes, microparticles, or microcapsules, or by administering it in linkage to a peptide that is known to enter the nucleus, or by administering it in linkage to a ligand subject to receptor-mediated endocytosis that can be used to target cell types specifically expressing the receptors (e.g., Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432), etc. In another embodiment, a nucleic acid-ligand complex can be formed in which the ligand comprises a fusogenic viral peptide that disrupts endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., International Patent Publications WO 92/06180; WO 92/22635; WO 92/20316; WO 93/14188; and WO 93/20221. Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

In a specific embodiment, a viral vector that contains the component protein encoding nucleic acids is used. For example, a retroviral vector can be used (Miller et al., 1993, Meth. Enzymol. 217:581-599). These retroviral vectors have been modified to delete retroviral sequences that are not necessary for packaging of the viral genome and integration into host cell DNA. The encoding nucleic acids to be used in gene therapy is/are cloned into the vector, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., 1994, Biotherapy 6:291-302, which describes the use of a retroviral vector to deliver the mdr1 gene to hematopoetic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are Clowes et al., 1994, J. Clin. Invest. 93:644-651; Kiem et al., 1994, Blood 83:1467-1473; Salmons and Gunzberg, 1993, Human Gene Therapy 4:129-141; and Grossman and Wilson, 1993, Curr. Opin. in Genetics and Devel. 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are the liver, the central nervous system, endothelial cells and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, Curr. Opin.

Genet. Devel. 3:499-503, discuss adenovirus-based gene therapy. The use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys has been demonstrated by Bout et al., 1994, Human Gene Therapy 5:3-10. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, Science 252:431-434; Rosenfeld et al., 1992, Cell 68:143-155; and Mastrangeli et al., 1993, J. Clin. Invest. 91:225-234.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, Proc. Soc. Exp. Biol. Med. 204:289-300.

Another approach to gene therapy involves transferring a gene into cells in tissue culture by methods such as electroporation, lipofection, calcium phosphate-mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene from these that have not. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art including, but not limited to, transfection by electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, 1993, Meth. Enzymol. 217:599-618; Cohen et al., 1993, Meth. Enzymol. 217:618-644; Cline, 1985, Pharmac. Ther. 29:69-92) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably, is heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. In a preferred embodiment, epithelial cells are injected, e.g., subcutaneously. In another embodiment, recombinant skin cells may be applied as a skin graft onto the patient. Recombinant blood cells (e.g., hematopoetic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes, blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, and granulocytes, various stem or progenitor cells, in particular hematopoetic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

-In-a-preferred-embodiment,-the-cell used-for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, a component protein encoding nucleic acid is/are introduced into the cells such that the gene or genes are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention. Such stem cells include but are not limited to hematopoetic stem cells (HSCs), stem cells of epithelial tissues such as the skin and the lining of the gut, embryonic heart muscle cells, liver stem cells (International Patent Publication WO 94/08598), and neural stem cells (Stemple and Anderson, 1992, Cell 71:973-985).

Epithelial stem cells (ESCs), or keratinocytes, can be obtained from tissues such as the skin and the lining of the gut by known procedures (Rheinwald, 1980, Meth. Cell Biol. 2A:229). In stratified epithelial tissue such as the skin, renewal occurs by mitosis of stem cells within the germinal layer, the layer closest to the basal lamina. Similarly, stem cells within the lining of the gut provide for a rapid renewal rate of this tissue. ESCs or keratinocytes obtained from the skin or lining of the gut of a patient or donor can be grown in tissue culture (Rheinwald, 1980, Meth. Cell Bio. 2A:229; Pittelkow and Scott, 1986, Mayo Clinic Proc. 61:771). If the ESCs are provided by a donor, a method for suppression of host versus graft reactivity (e.g., irradiation, or drug or antibody administration to promote moderate immunosuppression) can also be used.

With respect to hematopoetic stem cells (HSCs), any technique that provides for the isolation, propagation, and maintenance in vitro of HSCs can be used in this embodiment of the invention. Techniques by which this may be accomplished include (a) the isolation and establishment of HSC cultures from bone marrow cells isolated from the future host, or a donor, or (b) the use of previously established long-term HSC

cultures, which may be allogeneic or xenogeneic. Non-autologous HSCs are used preferably in conjunction with a method of suppressing transplantation immune reactions between the future host and patient. In a particular embodiment of the present invention, human bone marrow cells can be obtained from the posterior iliac crest by needle aspiration (see, e.g., Kodo et al., 1984, J. Clin. Invest. 73: 1377-1384). In a preferred embodiment of the present invention, the HSCs can be made highly enriched or in substantially pure form. This enrichment can be accomplished before, during, or after long-term culturing, and can be done by any technique known in the art. Long-term cultures of bone marrow cells can be established and maintained by using, for example, modified Dexter cell culture techniques (Dexter et al., 1977, J. Cell Physiol. 91:335) or Witlock-Witte culture techniques (Witlock and Witte, 1982, Proc. Natl. Acad. Sci. USA 79:3608-3612).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

Additional methods can be adapted for use to deliver a nucleic acid encoding the component proteins, or functional derivatives thereof, e.g., as described in Section 4.1, supra.

4.4.2 <u>USE OF ANTISENSE OLIGONUCLEOTIDES FOR SUPPRESSION OF PROTEIN COMPLEX/PROTEIN ACTIVITY</u>

In a specific embodiment of the present invention, protein complex activity and formation and protein activity is inhibited by use of antisense nucleic acids for the component proteins of the complex, that inhibit transcription and/or translation of their complementary sequence. The present invention provides the therapeutic or prophylactic use of nucleic acids of at least six nucleotides that are antisense to a gene or cDNA encoding a component protein, or a portion thereof. An "antisense" nucleic acid as used herein refers to a nucleic acid capable of hybridizing to a sequence-specific portion of a component protein RNA (preferably mRNA) by virtue of some sequence complementarity. The antisense nucleic acid may be complementary to a coding and/or noncoding region of a component protein mRNA. Such antisense nucleic acids that

inhibit complex formation or activity have utility as therapeutics, and can be used in the treatment or prevention of disorders as described supra.

double-stranded or single-stranded, RNA or DNA, or a modification or derivative thereof, which can be directly administered to a cell, or which can be produced intracellularly by transcription of exogenous, introduced sequences.

In another embodiment, the present invention is directed to a method for inhibiting -the-expression-of-component-protein-nucleic-acid-sequences, in a prokaryotic or eukaryotic cell, comprising providing the cell with an effective amount of a composition comprising an antisense nucleic acid of the component protein, or a derivative thereof, of the invention.

The antisense nucleic acids are of at least six nucleotides and are preferably oligonucleotides, ranging from 6 to about 200 nucleotides. In specific aspects, the oligonucleotide is at least 10 nucleotides, at least 15 nucleotides, at least 100 nucleotides, or at least 200 nucleotides. The oligonucleotides can be DNA or RNA or chimeric mixtures, or derivatives or modified versions thereof, and either single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone. The oligonucleotide may include other appending groups such as peptides, agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, Proc. Natl. Acad. Sci. USA 86:6553-6556; Lemaitre et al., 1987, Proc. Natl. Acad. Sci. USA 84:648-652; International Patent Publication No. WO 88/09810) or blood-brain barrier (see, e.g., International Patent Publication No. WO 89/10134), hybridization-triggered cleavage agents (see, e.g., Krol et al., 1988, BioTechniques 6:958-976), or intercalating agents (see, e.g., Zon, 1988, Pharm. Res. 5:539-549).

In a preferred aspect of the invention, an antisense oligonucleotide is provided, preferably as single-stranded DNA. The oligonucleotide may be modified at any position in its structure with constituents generally known in the art.

The antisense oligonucleotides may comprise at least one modified base moiety which is selected from the group including but not limited to 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl)uracil, 5-carboxymethylaminomethyl-2-thio-uridine, 5-carboxymethylaminomethyluracil, dihydrouracil, β -D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylguanine, 2,2-dimethylguanine,

2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, β-D-mannosylqueosine, 5N-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

In another embodiment, the oligonucleotide comprises at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the oligonucleotide comprises at least one modified phosphate backbone selected from the group consisting of a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphoramidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal, or an analog of the foregoing.

In yet another embodiment, the oligonucleotide is a 2-a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual ß-units, the strands run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641).

The oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

Oligonucleotides of the invention may be synthesized by standard methods known in the art, e.g., by use of an automated DNA synthesizer (such as are commercially avail-able from Biosearch, Applied Biosystems, etc.). As examples, phosphorothicate oligo-nucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. USA 85:7448-7451), etc.

In a specific embodiment, the antisense oligonucleotides comprise catalytic RNAs, or ribozymes (see, e.g., International Patent Publication No. WO 90/11364; Sarver et al., 1990, Science 247:1222-1225). In another embodiment, the oligonucleotide is a 2'-0-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res.

15:6131-6148), or a chimeric RNA-DNA analog (Inoue et al., 1987, FEBS Lett. 215:327-330).

In an alternative embodiment, the antisense nucleic acids of the invention are produced intracellularly by transcription from an exogenous sequence. For example, a vector can be introduced in vivo such that it is taken up by a cell, within which cell the vector or a portion thereof is transcribed, producing an antisense nucleic acid (RNA) of the invention. Such a vector would contain a sequence encoding the component protein. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors can be plasmid, viral, or others known in the art to be capable of replication and expression in mammalian cells. Expression of the sequences encoding the antisense RNAs can be by any promoter known in the art to act in mammalian, preferably human, cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter region (Bernoist and Chambon, 1981, Nature 290:304-310), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., 1980, Cell 22:787-797), the herpes thymidine kinase promoter (Wagner et al., 1981, Proc. Natl. Acad. Sci. USA 78:1441-1445), the regulatory sequences of the metallothionein gene (Brinster et al., 1982, Nature 296:39-42), etc.

The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a component protein gene, preferably a human gene. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," as referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with a component protein RNA it may contain and still form a stable duplex (or triplex, as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

The component protein antisense nucleic acids can be used to treat (or prevent) disorders of a cell type that expresses, or preferably overexpresses, a protein complex.

Cell types that express or overexpress component protein RNA can be identified by various methods known in the art. Such methods include, but are not limited to, hybridization with component protein-specific nucleic acids (e.g., by Northern blot hybridization, dot blot hybridization, or in situ hybridization), or by observing the ability of RNA from the cell type to be translated in vitro into the component protein by immunohistochemistry, Western blot analysis, ELISA, etc. In a preferred aspect, primary tissue from a patient can be assayed for protein expression prior to treatment, e.g., by immunocytochemistry, in situ hybridization, or any number of methods to detect protein or mRNA expression.

Pharmaceutical compositions of the invention (see Section 4.7, infra), comprising an effective amount of a protein component antisense nucleic acid in a pharmaceutically acceptable carrier can be administered to a patient having a disease or disorder that is of a type that expresses or overexpresses a protein complex of the present invention.

The amount of antisense nucleic acid that will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. Where possible, it is desirable to determine the antisense cytotoxicity in vitro, and then in useful animal model systems, prior to testing and use in humans.

In a specific embodiment, pharmaceutical compositions comprising antisense nucleic acids are administered via liposomes, microparticles, or microcapsules. In various embodiments of the invention, it may be useful to use such compositions to achieve sustained release of the antisense nucleic acids. In a specific embodiment, it may be desirable to utilize liposomes targeted via antibodies to specific identifiable central nervous system cell types (Leonetti et al., 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2448-2451; Renneisen et al., 1990, J. Biol. Chem. 265:16337-16342).

4.5 ASSAYS OF PROTEIN COMPLEXES/PROTEINS OF THE INVENTION AND DERIVATIVES AND ANALOGS THEREOF

The functional activity of a protein complex of the present invention, or a derivative, fragment or analog thereof or protein component thereof, can be assayed by various methods. Potential modulators (e.g., agonists and antagonists) of complex

activity or formation, e.g., anti- complex antibodies and antisense nucleic acids, can be assayed for the ability to modulate complex activity or formation.

In one embodiment of the present invention, where one is assaying for the ability to bind or compete with a wild-type complex for binding to an anti-complex antibody, various immunoassays known in the art can be used, including but not limited to competitive and non-competitive assay systems using techniques such linked immunosorbent radioimmunoassay, ELISA (enzyme assay), "sandwich" precipitin reactions. immunoassays. immunoradiometric assays, gel diffusion immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels), western blot analysis, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

The expression of the component protein genes (both endogenous and those expressed from cloned DNA containing the genes) can be detected using techniques known in the art, including but not limited to Southern hybridization (Southern, 1975, J. Mol. Biol. 98:503-517), northern hybridization (see, e.g., Freeman et al., 1983, Proc. Natl. Acad. Sci. USA 80:4094-4098), restriction endonuclease mapping (Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2nd Ed. Cold Spring Harbor Laboratory Press, New York), RNase protection assays (Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1997), DNA sequence analysis, and polymerase chain reaction amplification (PCR; U.S. Patent Nos. 4,683,202, 4,683,195, and 4,889,818; Gyllenstein et al., 1988, Proc. Natl. Acad. Sci. USA 85:7652-7657; Ochman et al., 1988, Genetics 120:621-623; Loh et al., 1989, Science 243:217-220) followed by Southern hybridization with probes specific for the component protein genes, in various cell types. Methods of amplification other than PCR commonly known in the art can be employed. In one embodiment, Southern hybridization can be used to detect genetic linkage of component protein gene mutations to physiological or pathological states. Various cell types, at various stages of development, can be characterized for their expression of component proteins at the same time and in the same cells. The stringency of the hybridization conditions for northern or Southern blot analysis can be manipulated to ensure detection of nucleic acids with the desired degree of relatedness to the specific probes used. Modifications to these methods and other methods commonly known in the art can be used.

Derivatives (e.g., fragments), homologs and analogs of one component protein can be assayed for binding to another component protein in the same complex by any method known in the art, for example the modified yeast matrix mating test described in Section 4.6.1 infra, immunoprecipitation with an antibody that binds to the component protein complexed with other component proteins in the same complex, followed by size fractionation of the immunoprecipitated proteins (e.g., by denaturing or nondenaturing polyacrylamide gel electrophoresis), Western blot analysis, etc.

One embodiment of the invention provides a method for screening a derivative, homolog or analog of a component protein for biological activity comprising contacting said derivative, homolog or analog of the component protein with the other component proteins in the same complex; and detecting the formation of a complex between said derivative, homolog or analog of the component protein and the other component proteins; wherein detecting formation of said complex indicates that said derivative, homolog or analog of has biological (e.g., binding) activity.

The invention also provides methods of modulating the activity of a component protein that can participate in a protein complex by administration of a binding partner of that protein or derivative, homolog or analog thereof.

In a specific embodiment of the present invention, a protein complex of the present invention is administered to treat or prevent a disease or disorder, since the complex and/or component proteins have been implicated in the disease and disorder. Accordingly, a protein complex or a derivative, homolog, analog or fragment thereof, nucleic acids encoding the component proteins, anti-complex antibodies, and other modulators of protein complex activity, can be tested for activity in treating or preventing a disease or disorder in in vitro and in vivo assays.

In one embodiment, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by contacting cultured cells that exhibit an indicator of the disease in vitro, with the therapeutic, and comparing the level of said indicator in the cells contacted with the therapeutic, with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the therapeutic has activity in treating or preventing the disease.

In another embodiment of the invention, a therapeutic of the invention can be assayed for activity in treating or preventing a disease by administering the therapeutic to a test animal-that is predisposed to develop symptoms of a disease, and measuring the change in said symptoms of the disease after administration of said therapeutic, wherein a reduction in the severity of the symptoms of the disease or prevention of the symptoms of the disease indicates that the therapeutic has activity in treating or preventing the disease. Such a test animal can be any one of a number of animal models known in the art for disease. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animal models to study any of the complexes provided in the invention.

4.6 <u>SCREENING FOR MODULATORS OF THE PROTEIN COMPLEXES/PROTEINS</u> OF THE INVENTION

A complex of the present invention, the component proteins of the complex and nucleic acids encoding the component proteins, as well as derivatives and fragments of the amino and nucleic acids, can be used to screen for compounds that bind to, or modulate the amount of, activity of, or protein component composition of, said complex, and thus, have potential use as modulators, i.e., agonists or antagonists, of complex activity, and/or complex formation, i.e., the amount of complex formed, and/or protein component composition of the complex.

Thus, the present invention is also directed to methods for screening for molecules that bind to, or modulate the function of, amount of, activity of, formation of or protein component composition of, a complex of the present invention. In one embodiment of the invention, the method for screening for a molecule that modulates directly or indirectly the function, activity or formation of a complex of the present invention comprises exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules under conditions conducive to modulation; and determining the amount of, the biochemical activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependend on the complex and/or the abundance and/or activity of a gene dependent on the complex in the presence of the one or more candidate

molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

In a further specific embodiment, a modulation of the formation process of a complex can be determined.

Such a modulation can either be a change in the typical time course of its formation or a change in the typical steps leading to the formation of the complete complex.

Such changes can for example be detected by analysing and comparing the process of complex formation in untreated wild type cells of a particular type and/or cells showing or having the predisposition to develop a certain disease phenotype and/or cells which have been treated with particular conditions and/or particular agents in a particular situation.

Methods to study such changes in time course are well known in the art and include for example Western-blot analysis of the proteins in the complex isolated at different steps of its formation.

Furthermore an aberrant intracellular localization of the protein complex and/or an abberant transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or a gene dependent on the complex can serve as a marker for a disease and thus have diagnostic utility for any disease which is caused by an aberrant activity, function, composition or formation of the complex of the invention.

Methods to study the intracellular localization are well known in the art and include, but are not limited to immunofluorescence analysis using antibodies specific for components of the protein. Preferentially, double-stainings including staining of other cellular structures are being used to facilitate the detection of the intracellular localization. Methods to analyse the transcription levels of a gene dependent on the complex are also well known in the art and include Northern blot analysis, quantitative PCR etc. The abundance of proteins dependent on the protein can be analyzed as described supra. Methods to study changes in the activity of proteins dependent on complex depend on the protein. The choice of such methods will be apparent to any person skilled in the art.

In another embodiment, the present invention further relates to a process for the identification and/or preparation of an effector of the complex comprising the step of bringing into contact a product of any of claims 1 to 8 with a compound, a mixture or a library of compounds and determining whether the compound or a certain compound of the mixture or library binds to the product and/or effects the products biological activity and optionally further purifying the compound positively tested as effector.

In another embodiment, the present invention is directed to a method for screening-for a -molecule-that-binds-a protein complex of the present invention comprising exposing said complex, or a cell or organism containing the complex machinery, to one or more candidate molecules; and determining whether said complex is bound by any of said candidate molecules. Such screening assays can be carried out using cell-free and cell-based methods that are commonly known in the art in vitro, in vivo or ex vivo. For example, an isolated complex can be employed, or a cell can be contacted with the candidate molecule and the complex can be isolated from such contacted cells and the isolated complex can be assayed for activity or component composition. In another example, a cell containing the complex can be contacted with the candidate molecule and the levels of the complex in the contacted cell can be measured. Additionally, such assays can be carried out in cells recombinantly expressing a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a component protein from fifth column of table 1, or a functionally active fragment or functionally active derivative thereof. Additionally, such assays can also be carried out in cells recombinantly expressing all component proteins from the group of proteins in the fifth column of table 1.

For example, assays can be carried out using recombinant cells expressing the protein components of a complex, to screen for molecules that bind to, or interfere with, or promote complex activity or formation. In preferred embodiments, polypeptide derivatives that have superior stabilities but retain the ability to form a complex (e.g., one or more component proteins modified to be resistant to proteolytic degradation in the binding assay buffers, or to be resistant to oxidative degradation), are used to screen for modulators of complex activity or formation. Such resistant molecules can be generated, e.g., by substitution of amino acids at proteolytic cleavage sites, the use of chemically derivatized amino acids at proteolytic susceptible sites, and the replacement of amino acid residues subject to oxidation, i.e. methionine and cysteine.

A particular aspect of the present invention relates to identifying molecules that inhibit or promote formation or degradation of a complex of the present invention, e.g., using the method described for isolating the complex and identifying members of the complex using the TAP assay described in Section 4, infra, and in WO 00/09716 and Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032, which are each incorporated by reference in their entirety. TNRF1

In another embodiment of the invention, a modulator is identified by administering a candidate molecule to a transgenic non-human animal expressing the complex component proteins from promoters that are not the native promoters of the respective proteins, more preferably where the candidate molecule is also recombinantly expressed in the transgenic non-human animal. Alternatively, the method for identifying such a modulator can be carried out in vitro, preferably with a purified complex, and a purified candidate molecule.

Agents/molecules (candidate molecules) to be screened can be provided as mixtures of a limited number of specified compounds, or as compound libraries, peptide libraries and the like. Agents/molecules to be screened may also include all forms of antisera, antisense nucleic acids, etc., that can modulate complex activity or formation. Exemplary candidate molecules and libraries for screening are set forth in Section 4.6.1, infra.

Screening the libraries can be accomplished by any of a variety of commonly known methods. See, e.g., the following references, which disclose screening of peptide libraries: Parmley and Smith, 1989, Adv. Exp. Med. Biol. 251:215-218; Scott and Smith, 1990, Science 249:386-390; Fowlkes et al., 1992, BioTechniques 13:422-427; Oldenburg et al., 1992, Proc. Natl. Acad. Sci. USA 89:5393-5397; Yu et al., 1994, Cell 76:933-945; Staudt et al., 1988, Science 241:577-580; Bock et al., 1992, Nature 355:564-566; Tuerk et al., 1992, Proc. Natl. Acad. Sci. USA 89:6988-6992; Ellington et al., 1992, Nature 355:850-852; U.S. Patent No. 5,096,815, U.S. Patent No. 5,223,409, and U.S. Patent No. 5,198,346, all to Ladner et al.; Rebar and Pabo, 1993, Science 263:671-673; and International Patent Publication No. WO 94/18318.

In a specific embodiment, screening can be carried out by contacting the library members with a complex immobilized on a solid phase, and harvesting those library members that bind to the protein (or encoding nucleic acid or derivative). Examples of such screening methods, termed "panning" techniques, are described by way of example in Parmley and Smith, 1988, Gene 73:305-318; Fowlkes et al., 1992, BioTechniques

13:422-427; International Patent Publication No. WO 94/18318; and in references cited hereinabove.

In a specific embodiment, fragments and/or analogs of protein components of a complex, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex formation (amount of complex or composition of complex) or activity in the cell, which thereby inhibit complex activity or formation in the cell.

In one embodiment, agents that modulate (i.e., antagonize or agonize) complex activity or formation can be screened for using a binding inhibition assay, wherein agents are screened for their ability to modulate formation of a complex under aqueous, or physiological, binding conditions in which complex formation occurs in the absence of the agent to be tested. Agents that interfere with the formation of complexes of the invention are identified as antagonists of complex formation. Agents that promote the formation of complexes are identified as agonists of complex formation. Agents that completely block the formation of complexes are identified as inhibitors of complex formation.

Methods for screening may involve labeling the component proteins of the complex with radioligands (e.g., 125 I or 3 H), magnetic ligands (e.g., paramagnetic beads covalently attached to photobiotin acetate), fluorescent ligands (e.g., fluorescein or rhodamine), or enzyme ligands (e.g., luciferase or β -galactosidase). The reactants that bind in solution can then be isolated by one of many techniques known in the art, including but not restricted to, co-immunoprecipitation of the labeled complex moiety using antisera against the unlabeled binding partner (or labeled binding partner with a distinguishable marker from that used on the second labeled complex moiety), immunoaffinity chromatography, size exclusion chromatography, and gradient density centrifugation. In a preferred embodiment, the labeled binding partner is a small fragment or peptidomimetic that is not retained by a commercially available filter. Upon binding, the labeled species is then unable to pass through the filter, providing for a simple assay of complex formation.

Methods commonly known in the art are used to label at least one of the component members of the complex. Suitable labeling methods include, but are not limited to, radiolabeling by incorporation of radiolabeled amino acids, e.g., ³H-leucine or ³⁵S-methionine, radiolabeling by post-translational iodination with ¹²⁵I or ¹³¹I using the chloramine T method, Bolton-Hunter reagents, etc., or labeling with ³²P using phosphorylase and inorganic radiolabeled phosphorous, biotin labeling with photobiotin-

acetate and sunlamp exposure, etc. In cases where one of the members of the complex is immobilized, e.g., as described infra, the free species is labeled. Where neither of the interacting species is immobilized, each can be labeled with a distinguishable marker such that isolation of both moieties can be followed to provide for more accurate quantification, and to distinguish the formation of homomeric from heteromeric complexes. Methods that utilize accessory proteins that bind to one of the modified interactants to improve the sensitivity of detection, increase the stability of the complex, etc., are provided.

Typical binding conditions are, for example, but not by way of limitation, in an aqueous salt solution of 10-250 mM NaCl, 5-50 mM Tris-HCl, pH 5-8, and 0.5% Triton X-100 or other detergent that improves specificity of interaction. Metal chelators and/or divalent cations may be added to improve binding and/or reduce proteolysis. Reaction temperatures may include 4, 10, 15, 22, 25, 35, or 42 degrees Celsius, and time of incubation is typically at least 15 seconds, but longer times are preferred to allow binding equilibrium to occur. Particular complexes can be assayed using routine protein binding assays to determine optimal binding conditions for reproducible binding.

The physical parameters of complex formation can be analyzed by quantification of complex formation using assay methods specific for the label used, e.g., liquid scintillation counting for radioactivity detection, enzyme activity for enzyme-labeled moieties, etc. The reaction results are then analyzed utilizing Scatchard analysis, Hill analysis, and other methods commonly known in the arts (see, e.g., Proteins, Structures, and Molecular Principles, 2nd Edition (1993) Creighton, Ed., W.H. Freeman and Company, New York).

In a second common approach to binding assays, one of the binding species is immobilized on a filter, in a microtiter plate well, in a test tube, to a chromatography matrix, etc., either covalently or non-covalently. Proteins can be covalently immobilized using any method well known in the art, for example, but not limited to the method of Kadonaga and Tjian, 1986, Proc. Natl. Acad. Sci. USA 83:5889-5893, i.e., linkage to a cyanogen-bromide derivatized substrate such as CNBr-Sepharose 4B (Pharmacia). Where needed, the use of spacers can reduce steric hindrance by the substrate. Non-covalent attachment of proteins to a substrate include, but are not limited to, attachment of a protein to a charged surface, binding with specific antibodies, binding to a third unrelated interacting protein, etc.

Assays of agents (including cell extracts or a library pool) for competition for binding of one member of a complex (or derivatives thereof) with another member of the complex labeled by any means (e.g., those means described above) are provided to screen for competitors or enhancers of complex formation.

In specific embodiments, blocking agents to inhibit non-specific binding of reagents to other protein components, or absorptive losses of reagents to plastics, immobilization matrices, etc., are included in the assay mixture. Blocking agents include, but are not restricted to bovine serum albumin, β-casein, nonfat dried milk, Denhardt's reagent, Ficoll, polyvinylpyrolidine, nonionic detergents (NP40, Triton X-100, Tween 20, Tween 80, etc.), ionic detergents (e.g., SDS, LDS, etc.), polyethylene glycol, etc. Appropriate blocking agent concentrations allow complex formation.

After binding is performed, unbound, labeled protein is removed in the supernatant, and the immobilized protein retaining any bound, labeled protein is washed extensively. The amount of bound label is then quantified using standard methods in the art to detect the label as described, supra.

In another specific embodiments screening for modulators of the protein complexes/protein as provided herein can be carried out by attaching those and/or the antibodies as provided herein to a solid carrier. In a further specific embodiment, the invention relates to an array of said molecules.

The preparation of such an array containing different types of proteins, including antibodies) is well known in the art and is apparent to a person skilled in the art (see e.g. Ekins et al., 1989, J. Pharm. Biomed. Anal. 7:155-168; Mitchell et al. 2002, Nature Biotechnol. 20:225-229; Petricoin et al., 2002, Lancet 359:572-577; Templin et al., 2001, Trends Biotechnol. 20:160-166; Wilson and Nock, 2001, Curr. Opin. Chem. Biol. 6:81-85; Lee et al., 2002 Science 295:1702-1705; MacBeath and Schreiber, 2000, Science 289:1760; Blawas and Reichert, 1998, Biomaterials 19:595; Kane et al., 1999, Biomaterials 20:2363; Chen et al., 1997, Science 276:1425; Vaugham et al., 1996, Nature Biotechnol. 14:309-314; Mahler et al., 1997, Immunotechnology 3:31-43; Roberts et al., 1999, Curr. Opin. Chem. Biol. 3:268-273; Nord et al., 1997, Nature Biotechnol. 15:772-777; Nord et al., 2001, Eur. J. Biochem. 268:4269-4277; Brody and Gold, 2000, Rev. Mol. Biotechnol. 74:5-13; Karlstroem and Nygren, 2001, Anal. Biochem. 295:22-30; Nelson et al., 2000, Electrophoresis 21:1155-1163; Honore et al., 2001, Expert Rev. Mol. Diagn. 3:265-274; Albala, 2001, Expert Rev. Mol. Diagn. 2:145-152, Figeys and Pinto, 2001, Electrophoresis 2:208-216 and references in the publications listed here).

Complexes can be attached to an array by different means as will be apparent to a person skilled in the art. Complexes can for example be added to the array via a TAP-tag (as described in WO/0009716 and in Rigaut et al., 1999, Nature Biotechnol. 10:1030-1032) after the purification step or by another suitable purification scheme as will be apparent to a person skilled in the art.

Optionally, the proteins of the complex can be cross-linked to enhance the stability of the complex. Different methods to cross-link proteins are well known in the art. Reactive end-groups of cross-linking agents include but are not limited to -COOH, -SH, -NH2 or N-oxy-succinamate.

The spacer of the cross-linking agent should be chosen with respect to the size of the complex to be cross-linked. For small protein complexes, comprising only a few proteins, relatively short spacers are preferable in order to reduce the likelihood of cross-linking separate complexes in the reaction mixture. For larger protein complexes, additional use of larger spacers is preferable in order to facilitate cross-linking between proteins within the complex.

It is preferable to check the success-rate of cross-linking before linking the complex to the carrier.

As will be apparent to a person skilled in the art, the optimal rate of cross-linking need to be determined on a case by case basis. This can be achieved by methods well known in the art, some of which are exemplary described below.

A sufficient rate of cross-linking can be checked f.e. by analysing the cross-linked complex vs. a non-cross-linked complex on a denaturating protein gel.

If cross-linking has been performed successfully, the proteins of the complex are expected to be found in the same lane, whereas the proteins of the non-cross-linked complex are expected to be separated according to their individual characteristics. Optionally the presence of all proteins of the complex can be further checked by peptide-sequencing of proteins in the respective bands using methods well known in the art such as mass spectrometry and/or Edman degradation.

In addition, a rate of crosslinking which is too high should also be avoided. If cross-linking has been carried out too extensively, there will be an increasing amount of cross-linking of the individual protein complex, which potentially interferes with a screening for potential binding partners and/or modulators etc. using the arrays.

The presence of such structures can be determined by methods well known in the art and include e.g. gel-filtration experiments comparing the gel filtration profile solutions containing cross-linked complexes vs. uncross-linked complexes.

Optionally, functional assays as will be apparent to a person skilled in the art, some of which are exemplarily provided herein, can be performed to check the integrity of the complex.

-Alternatively, members-of-the-protein complex can be expressed as a single fusion protein and coupled to the matrix as will be apparent to a person skilled in the art.

Optionally, the attachment of the complex or proteins or antibody as outlined above can be further monitored by various methods apparent to a person skilled in the art. Those include, but are not limited to surface plasmon resonance (see e.g. McDonnel, 2001, Curr. Opin. Chem. Biol. 5:572-577; Lee, 2001, Trends Biotechnol. 19:217-222; Weinberger et al., 2000, 1:395-416; Pearson et al., 2000, Ann. Clin. Biochem. 37:119-145; Vely et al., 2000, Methods Mol. Biol. 121:313-321; Slepak, 2000, J. Mol Recognit. 13:20-26.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Fe65-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Fe65-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Biederer Thomas et al., 2002, J Neurosci, 22:7340-51.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the X11b-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA)

and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the PSEN2 -complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the PSEN2 -complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Nicastrin-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Nicastrin-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting

proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Aph-1a-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Aph-1a-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the Pen-2-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Pen-2-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the APP695SW-complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP695SW-complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Vassar R et al., 1999, Science, 286:735-41.

Exemplary assays useful for measuring the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA)

and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Yan R et al., 1999, Nature, 402:533-7.

Exemplary assays useful for measuring the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting of the APP-C99 -complex include but are not limited to those described in Tian Gaochao et al., 2002, J Biol Chem, 277:31499-505.

Exemplary assays useful for measuring transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the APP-C99 -complex include but are not limited to those described in Cao X et al., 2001, Science, 293:115-20.

Exemplary assays useful for measuring the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau-complex include but are not limited to those described in Drewes G et al., 1997, Cell, 89:297-308.

Exemplary assays useful for measuring the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) of the Tau-complex include but are not limited to those described in Barghorn S et al., 2000, Biochemistry, 39:11714-21.

4.6.1 CANDIDATE MOLECULES

Any molecule known in the art can be tested for its ability to modulate (increase or decrease) the amount of, activity of, or protein component composition of a complex of the present invention as detected by a change in the amount of, activity of, or protein component composition of, said complex. By way of example, a change in the amount of the complex can be detected by detecting a change in the amount of the complex that can be isolated from a cell expressing the complex machinery. For identifying a molecule that modulates complex activity, candidate molecules can be directly provided to a cell expressing the complex machinery, or, in the case of candidate proteins, can be

provided by providing their encoding nucleic acids under conditions in which the nucleic acids are recombinantly expressed to produce the candidate proteins within the cell expressing the complex machinery, the complex is then isolated from the cell and the isolated complex is assayed for activity using methods well known in the art, not limited to those described, supra.

This embodiment of the invention is well suited to screen chemical libraries for molecules which modulate, e.g., inhibit, antagonize, or agonize, the amount of, activity of, or protein-component composition-of the complex. The chemical libraries can be peptide libraries, peptidomimetic libraries, chemically synthesized libraries, recombinant, e.g., phage display libraries, and in vitro translation-based libraries, other non-peptide synthetic organic libraries, etc.

Exemplary libraries are commercially available from several sources (ArQule, Tripos/PanLabs, ChemDesign, Pharmacopoeia). In some cases, these chemical libraries are generated using combinatorial strategies that encode the identity of each member of the library on a substrate to which the member compound is attached, thus allowing direct and immediate identification of a molecule that is an effective modulator. Thus, in many combinatorial approaches, the position on a plate of a compound specifies that compound's composition. Also, in one example, a single plate position may have from 1-20 chemicals that can be screened by administration to a well containing the interactions of interest. Thus, if modulation is detected, smaller and smaller pools of interacting pairs can be assayed for the modulation activity. By such methods, many candidate molecules can be screened.

Many diversity libraries suitable for use are known in the art and can be used to provide compounds to be tested according to the present invention. Alternatively, libraries can be constructed using standard methods. Chemical (synthetic) libraries, recombinant expression libraries, or polysome-based libraries are exemplary types of libraries that can be used.

The libraries can be constrained or semirigid (having some degree of structural rigidity), or linear or nonconstrained. The library can be a cDNA or genomic expression library, random peptide expression library or a chemically synthesized random peptide library, or non-peptide library. Expression libraries are introduced into the cells in which the assay occurs, where the nucleic acids of the library are expressed to produce their encoded proteins.

In one embodiment, peptide libraries that can be used in the present invention may be libraries that are chemically synthesized in vitro. Examples of such libraries are given in Houghten et al., 1991, Nature 354:84-86, which describes mixtures of free hexapeptides in which the first and second residues in each peptide were individually and specifically defined; Lam et al., 1991, Nature 354:82-84, which describes a "one bead, one peptide" approach in which a solid phase split synthesis scheme produced a library of peptides in which each bead in the collection had immobilized thereon a single. random sequence of amino acid residues; Medynski, 1994, Bio/Technology 12:709-710. which describes split synthesis and T-bag synthesis methods; and Gallop et al., 1994, J. Med. Chem. 37:1233-1251. Simply by way of other examples, a combinatorial library may be prepared for use, according to the methods of Ohlmeyer et al., 1993, Proc. Natl. Acad. Sci. USA 90:10922-10926; Erb et al., 1994, Proc. Natl. Acad. Sci. USA 91:11422-11426; Houghten et al., 1992, Biotechniques 13:412; Jayawickreme et al., 1994, Proc. Natl. Acad. Sci. USA 91:1614-1618; or Salmon et al., 1993, Proc. Natl. Acad. Sci. USA 90:11708-11712. PCT Publication No. WO 93/20242 and Brenner and Lerner, 1992, Proc. Natl. Acad. Sci. USA 89:5381-5383 describe "encoded combinatorial chemical libraries," that contain oligonucleotide identifiers for each chemical polymer library member.

In a preferred embodiment, the library screened is a biological expression library that is a random peptide phage display library, where the random peptides are constrained (e.g., by virtue of having disulfide bonding).

Further, more general, structurally constrained, organic diversity (e.g., nonpeptide) libraries, can also be used. By way of example, a benzodiazepine library (see e.g., Bunin et al., 1994, Proc. Natl. Acad. Sci. USA 91:4708-4712) may be used.

Conformationally constrained libraries that can be used include but are not limited to those containing invariant cysteine residues which, in an oxidizing environment, crosslink by disulfide bonds to form cystines, modified peptides (e.g., incorporating fluorine, metals, isotopic labels, are phosphorylated, etc.), peptides containing one or more non-naturally occurring amino acids, non-peptide structures, and peptides containing a significant fraction of -carboxyglutamic acid.

Libraries of non-peptides, e.g., peptide derivatives (for example, that contain one or more non-naturally occurring amino acids) can also be used. One example of these are peptoid libraries (Simon et al., 1992, Proc. Natl. Acad. Sci. USA 89:9367-9371). Peptoids are polymers of non-natural amino acids that have naturally occurring side

chains attached not to the α carbon but to the backbone amino nitrogen. Since peptoids are not easily degraded by human digestive enzymes, they are advantageously more easily adaptable to drug use. Another example of a library that can be used, in which the amide functionalities in peptides have been permethylated to generate a chemically transformed combinatorial library, is described by Ostresh et al., 1994, Proc. Natl. Acad. Sci. USA 91:11138-11142).

The members of the peptide libraries that can be screened according to the invention are not limited to containing the 20 naturally occurring amino acids. In particular, chemically synthesized libraries and polysome based libraries allow the use of amino acids in addition to the 20 naturally occurring amino acids (by their inclusion in the precursor pool of amino acids used in library production). In specific embodiments, the library members contain one or more non-natural or non-classical amino acids or cyclic peptides. Non-classical amino acids include but are not limited to the D-isomers of the common amino acids, -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid; -Abu, -Ahx, 6-amino hexanoic acid; Aib, 2-amino isobutyric acid; 3-amino propionic acid; ornithine; norleucine; norvaline, hydroxyproline, sarcosine, citrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, B-alanine, designer amino acids such as B-methyl amino acids, C-methyl amino acids, N-methyl amino acids, fluoro-amino acids and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

In a specific embodiment, fragments and/or analogs of complexes of the invention, or protein components thereof, especially peptidomimetics, are screened for activity as competitive or non-competitive inhibitors of complex activity or formation.

In another embodiment of the present invention, combinatorial chemistry can be used to identify modulators of a the complexes. Combinatorial chemistry is capable of creating libraries containing hundreds of thousands of compounds, many of which may be structurally similar. While high throughput screening programs are capable of screening these vast libraries for affinity for known targets, new approaches have been developed that achieve libraries of smaller dimension but which provide maximum chemical diversity. (See e.g., Matter, 1997, J. Med. Chem. 40:1219-1229).

One method of combinatorial chemistry, affinity fingerprinting, has previously been used to test a discrete library of small molecules for binding affinities for a defined panel of proteins. The fingerprints obtained by the screen are used to predict the affinity of the individual library members for other proteins or receptors of interest (in the instant

invention, the protein complexes of the present invention and protein components thereof.) The fingerprints are compared with fingerprints obtained from other compounds known to react with the protein of interest to predict whether the library compound might similarly react. For example, rather than testing every ligand in a large library for interaction with a complex or protein component, only those ligands having a fingerprint similar to other compounds known to have that activity could be tested. (See, e.g., Kauvar et al., 1995, Chem. Biol. 2:107-118; Kauvar, 1995, Affinity fingerprinting, Pharmaceutical Manufacturing International. 8:25-28; and Kauvar, Toxic-Chemical Detection by Pattern Recognition in New Frontiers in Agrochemical Immunoassay, Kurtz, Stanker and Skerritt (eds), 1995, AOAC: Washington, D.C., 305-312).

Kay et al. (1993, Gene 128:59-65) disclosed a method of constructing peptide libraries that encode peptides of totally random sequence that are longer than those of any prior conventional libraries. The libraries disclosed in Kay et al. encode totally synthetic random peptides of greater than about 20 amino acids in length. Such libraries can be advantageously screened to identify complex modulators. (See also U.S. Patent No. 5,498,538 dated March 12, 1996; and PCT Publication No. WO 94/18318 dated August 18, 1994).

A comprehensive review of various types of peptide libraries can be found in Gallop et al., 1994, J. Med. Chem. 37:1233-1251.

4.7 PHARMACEUTICAL COMPOSITIONS AND THERAPEUTIC/PROPHYLACTIC ADMINISTRATION

The invention provides methods of treatment (and prophylaxis) by administration to a subject of an effective amount of a therapeutic of the invention. In a preferred aspect, the therapeutic is substantially purified. The subject is preferably an animal including, but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human. In a specific embodiment, a non-human mammal is the subject.

Various delivery systems are known and can be used to administer a therapeutic of the invention, e.g., encapsulation in liposomes, microparticles, and microcapsules: use of recombinant cells capable of expressing the therapeutic, use of receptor-mediated endocytosis (e.g., Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432); construction of a

therapeutic nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion, by bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral, rectal and intestinal mucosa, etc.), and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment. This may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) of a malignant tumor or neoplastic or preneoplastic tissue.

In another embodiment, the therapeutic can be delivered in a vesicle, in particular a liposome (Langer, 1990, Science 249:1527-1533; Treat et al., 1989, In: Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler, eds., Liss, New York, pp. 353-365; Lopez-Berestein, ibid., pp. 317-327; see generally ibid.)

In yet another embodiment, the therapeutic can be delivered via a controlled release system. In one embodiment, a pump may be used (Langer, supra; Sefton, 1987, CRC Crit. Ref. Biomed. Eng. 14:201-240; Buchwald et al., 1980, Surgery 88:507-516; Saudek et al., 1989, N. Engl. J. Med. 321:574-579). In another embodiment, polymeric materials can be used (Medical Applications of Controlled Release, Langer and Wise, eds., CRC Press, Boca Raton, Florida, 1974; Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball, eds., Wiley, New York, 1984; Ranger and Peppas, 1983, Macromol. Sci. Rev. Macromol. Chem. 23:61; Levy et al., 1985, Science 228:190-192; During et al., 1989, Ann. Neurol. 25:351-356; Howard et al.,

1989, J. Neurosurg. 71:858-863). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (e.g., Goodson, 1984, In: Medical Applications of Controlled Release, supra, Vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer (1990, Science 249:1527-1533).

In a specific embodiment where the therapeutic is a nucleic acid encoding a protein therapeutic, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or by coating it with lipids, cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (e.g., Joliot et al., 1991, Proc. Natl. Acad. Sci. USA 88:1864-1868), etc. Alternatively, a nucleic acid therapeutic can be introduced intracellularly and incorporated by homologous recombination within host cell DNA for expression.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a therapeutic, and a pharmaceutically acceptable carrier. In a specific embodiment, "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are preferred carriers when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are preferably employed as liquid carriers for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH

buffering agents. These compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the therapeutic, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated, in accordance with routine procedures, as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water-free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water or saline for injection can be provided so that the ingredients may be mixed prior to administration.

The therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free carboxyl groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., those formed with free amine groups such as those derived from isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc., and those derived from sodium, potassium, ammonium, calcium, and ferric hydroxides, etc.

The amount of the therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise

dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20-500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. For example, the kit can comprise in one or more containers a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins listed in the fourth column of table 1; and a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1.

Alternatively, the kit can comprise in one or more containers, all proteins, functionally active fragments or functionally active derivatives thereof of from the group of proteins in the sixth column of table 1.

The kits of the present invention can also contain expression vectors encoding the essential components of the complex machinery, which components after being expressed can be reconstituted in order to form a biologically active complex. Such a kit preferably also contains the required buffers and reagents. Optionally associated with such container(s) can be instructions for use of the kit and/or a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of

pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

4.8 ANIMAL MODELS

The present invention also provides animal models. In one embodiment, animal models for diseases and disorders involving the protein complexes of the present invention are provided. These animal models are well known in the art. These animal models include, but are not limited to those which are listed in the section 4.6 (supra) as exemplary animald models to study any of the complexes provided in the invention. Such animals can be initially produced by promoting homologous recombination or insertional mutagenesis between genes encoding the protein components of the complexes in the chromosome, and exogenous genes encoding the protein components of the complexes that have been rendered biologically inactive or deleted (preferably by insertion of a heterologous sequence, e.g., an antibiotic resistance gene). In a preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which a gene encoding a component protein from the fourth column of table 1, or a functionally active fragment or functionally active derivative thereof, and a gene encoding a component protein from the fifth column of table 1, or a functionally active fragment or functionally active derivative thereof, has been inactivated or deleted (Capecchi, 1989, Science 244:1288-1292).

In another preferred aspect, homologous recombination is carried out by transforming embryo-derived stem (ES) cells with one or more vectors containing one or more insertionally inactivated genes, such that homologous recombination occurs, followed by injecting the transformed ES cells into a blastocyst, and implanting the blastocyst into a foster mother, followed by the birth of the chimeric animal ("knockout animal") in which the genes of all component proteins from the group of proteins listed in the fourth column of table 1 or of all proteins from the group of proteins listed in the fifth column of table 1 have been inactivated or deleted.

The chimeric animal can be bred to produce additional knockout animals. Such animals can be mice, hamsters, sheep, pigs, cattle, etc., and are preferably non-human mammals. In a specific embodiment, a knockout mouse is produced.

Such knockout animals are expected to develop, or be predisposed to developing, diseases or disorders associated with mutations involving the protein complexes of the present invention, and thus, can have use as animal models of such diseases and disorders, e.g., to screen for or test molecules (e.g., potential therapeutics) for such diseases and disorders.

In a different embodiment of the invention, transgenic animals that have incorporated and express (or over-express or mis-express) a functional gene encoding a protein component of the complex, e.g. by introducing the a gene encoding one or more of the components of the complex under the control of a heterologous promoter (i.e., a promoter that is not the native promoter of the gene) that either over-expresses the protein or proteins, or expresses them in tissues not normally expressing the complexes or proteins, can have use as animal models of diseases and disorders characterized by elevated levels of the protein complexes. Such animals can be used to screen or test molecules for the ability to treat or prevent the diseases and disorders cited supra.

In one embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group of proteins listed in the fourth column of table 1, and and endogenous gene encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins listed in the fifth column of table 1 has been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof. In addition, the present invention provides a recombinant non-human animal in which the endogenous genes of all proteins, or functionally active fragments or functionally active derivatives thereof of one of the group of proteins listed in the sixth column have been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof:

In another embodiment, the present invention provides a recombinant non-human animal in which an endogenous gene encoding a first protein, or a functionally active fragment or functionally active derivative thereof, which first protein is selected from the group consisting of proteins of the fourth column of table 1, and endogenous gene

encoding a second protein, or a functionally active fragment or functionally active derivative thereof, which second protein is selected from the group consisting of proteins of the fifth column, of table 1 are recombinantly expressed in said animal or an ancestor thereof.

The following series of examples are presented by way of illustration and not by way of limitation on the scope of the invention.

EXAMPLES

An object of the present invention was to identify protein complexes of the APP processing pathway, component proteins of the said complexes, fragments and derivatives of the component proteins, and antibodies specific to the complexes. The present invention also relates to methods for use of the complexes of the APP processing pathway and their interacting proteins in, inter alia, screening, diagnosis, and therapy, as well as to methods of preparing the complexes.

By applying the process according to the invention said complexes were identified. The components are listed in table 1.

Those complexes are, as called herein, the following complexes:

Aph1a-complex, APP-695SW-complex, APP-C99-complex, Fe65-complex, Nicastrin-complex, Psen-2-complex, Pen2-complex, Tau-complex, X11B-complex

Thus, the invention relates to the following embodiments:

The present invention relates to the Fe65-complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a

nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and
- (vii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein

eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,

- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally-active-fragment thereof, or a homolog-thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (viii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (ix) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (x) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xiii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, (xiv) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, (xv) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xvi) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and

(xvii) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured

salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 2. The protein complex according to No. 1 wherein the first protein is the protein Fe65 (SEQ ID NO. 13), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Fe65' encoded by a nucleic acid that hybridizes to the 'Fe65' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3"

protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,

- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
 - (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
 - (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
 - (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
 - (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid

that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,

(xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,

(xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a

nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein

tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,

- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a

nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to

probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

- (xxi) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.
- 4. The protein complex according to No. 1 comprising all but 1 16 of the following proteins:
- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,

- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,

- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by-a nucleic-acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions.
- (xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions.

- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the

production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of the Fe65 complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the Fe65 complex selected from
- (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that

hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

- (iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and
- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% FicoII, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatiory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.

- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- (iii) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatiory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (ii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,
- -(iii)-"Protein-similar-to-probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, comprising the steps of (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of (a) exposing said complex, or a cell or organism containing Fe65 complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a

protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or

- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or

(xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions, and/or

(xv) "iPl00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPl00104084.1" encoded by a nucleic acid that hybridizes to the "IPl00104084.1" nucleic acid or its complement under low stringency conditions, and/or

(xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

- (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatiory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammationy diseases such as chronic

inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.

- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions, and/or (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions, and/or

its complement under low stringency conditions, and/or

- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or

- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that

hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription factor CP2" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, is present in the complex.

- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatiory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins
- (i) "14-3-3 protein epsilon" (SEQ ID No:1) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein epsilon" encoded by a nucleic acid that hybridizes to the "14-3-3 protein epsilon" nucleic acid or its complement under low stringency conditions,
- (ii) "14-3-3 protein beta/alpha" (SEQ ID No:2) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein beta/alpha" encoded by a nucleic acid that hybridizes to the "14-3-3 protein beta/alpha" nucleic acid or its complement under low stringency conditions,
- (iii) "14-3-3 protein eta" (SEQ ID No:3) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein eta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein eta" nucleic acid or its complement under low stringency conditions,
- (iv) "14-3-3 protein gamma" (SEQ ID No:4) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein gamma" encoded by a nucleic acid that hybridizes to the "14-3-3 protein gamma" nucleic acid or its complement under low stringency conditions,
- (v) "14-3-3 protein tau" (SEQ ID No:5) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein tau" encoded by a nucleic acid that hybridizes to the "14-3-3 protein tau" nucleic acid or its complement under low stringency conditions,
- (vi) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (vii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (viii) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a

nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (ix) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (x) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (xi) "ATP-binding cassette, sub-family B, member 7" (SEQ ID No:11) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family B, member 7" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family B, member 7" nucleic acid or its complement under low stringency conditions,
- (xii) "ECP-51" (SEQ ID No:12) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECP-51" encoded by a nucleic acid that hybridizes to the "ECP-51" nucleic acid or its complement under low stringency conditions,
- (xiii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (xiv) "GAP-associated tyrosine phosphoprotein p62" (SEQ ID No:14) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GAP-associated tyrosine phosphoprotein p62" encoded by a nucleic acid that hybridizes to the "GAP-associated tyrosine phosphoprotein p62" nucleic acid or its complement under low stringency conditions,
- (xv) "IPI00104084.1" (SEQ ID No:15) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IPI00104084.1" encoded by a nucleic acid that hybridizes to the "IPI00104084.1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xvii) "Krab box protein ensp00000302970" (SEQ ID No:17) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Krab box protein ensp00000302970" encoded by a nucleic acid that hybridizes to the "Krab box protein ensp00000302970" nucleic acid or its complement under low stringency conditions,

(xviii) "PDZ domain protein MAGI-3" (SEQ ID No:18) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ domain protein MAGI-3" encoded by a nucleic acid that hybridizes to the "PDZ domain protein MAGI-3" nucleic acid or its complement under low stringency conditions, (xix) "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA (PP2A, 55 kDa regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, (xx) "Protein similar to probable mitotic centromere associated kinesin" (SEQ ID No:20) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" encoded by a nucleic acid that hybridizes to the "Protein similar to probable mitotic centromere associated kinesin" nucleic acid or its complement under low stringency conditions,

(xxi) "RNB6" (SEQ ID No:21) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNB6" encoded by a nucleic acid that hybridizes to the "RNB6" nucleic acid or its complement under low stringency conditions,

(xxii) "SAP-62" (SEQ ID No:22) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SAP-62" encoded by a nucleic acid that hybridizes to the "SAP-62" nucleic acid or its complement under low stringency conditions,

(xxiii) "Transcription factor CP2" (SEQ ID No:23) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Transcription factor CP2" encoded by a nucleic acid that hybridizes to the "Transcription

factor CP2" nucleic acid or its complement under low stringency conditions, and/or(xxiv) "Zinc finger protein 277" (SEQ ID No:24) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 277" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 277" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatiory diseases such as chronic inflammatory disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer.

The invention further relates to the following embodiments of the X11beta-complex:

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions.
- (ii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,
- (iii) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (iv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
- (v) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a

nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and

- (vi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (iv) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (v) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vi) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (vii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (viii) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (x) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xi) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,
- (xii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiii) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

- (xiv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xv) "Dynein light chain 2A" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A" encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,
- (xvii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,
- (xviii) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xix) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,
- (xx) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xxi) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiii) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, (xxiv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxv) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxvii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxiii) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxv) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxvi) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxxviii)_"KIAA0564" (SEQ ID No:62) or a functionally_active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

- (xxxix) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xl) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,
- (xli) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xlii) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,
- (xliii) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xliv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xlv) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB"

encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlvi) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xlviii) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,

- (xlix) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (I) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (li) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (lii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (liii) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)"

encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, (liv) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

- (iv) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,
- (Ivi) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (Ivii) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (Iviii) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lix) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, (Ix) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxi) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a

nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions.

(lxii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixiii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxiv) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, (lxv) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxvi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxvii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(Ixviii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(ixix) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxx) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and

(lxxi) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 2. The protein complex according to No. 1 wherein the first protein is the protein X11beta (SEQ ID NO. 96), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'X11beta' encoded by a nucleic acid that hybridizes to the 'X11beta' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,

- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1"

encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,

- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions.
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A" encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A" nucleic acid or its complement under low stringency conditions,

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,
- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" --- encoded-by-a-nucleic-acid-that-hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a"

encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions.

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xlii) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,
- (xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,
- (xiv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (I) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (Iv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

- (Ivi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, (Ivii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,
- (Iviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,
- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a

nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,

(lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(Ixvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(ixix) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, (Ixx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a

nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, and a protein complex selected from complex (II) and comprising the following proteins: (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19"

- encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions.
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,

- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light

chain 2A " encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A " nucleic acid or its complement under low stringency conditions,

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxiv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxv) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvi) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxxix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564"

encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

- (xl) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xli) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,
- (xlii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xliii) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,
- (xliv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xlv) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xivi) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,
- (xlvii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a

nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

- (xlviii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (xlix) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (I) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions.
- (li) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (lii) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (liii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (liv) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions,
- (Iv) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

- (Ivi) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions.
- (Ivii) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (Iviii) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (lix) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lx) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, (lxi) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxiii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2"

encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(lxiv) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxv) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, (lxvi) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(Ixvii) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxviii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(lxix) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxx) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(lxxi) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or-its-complement under low stringency conditions, and/or

(lxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions.

- 4. The protein complex according to No. 1 comprising all but 1 70 of the following proteins:
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,

- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes

to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,

(xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,

(xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,

(xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,

(xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A" encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A" nucleic acid or its complement under low stringency conditions,

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,

(xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a

nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

- (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xlii) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,
- (xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin,

gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,

(xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,

(xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

- (I) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,

- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions.
- (Iiii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (Iv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,
- (Ivi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, (Ivii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,
- (Iviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions.
- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions,
- (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
 - (Ixi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a
- —functionally-active-fragment thereof, or a homolog-thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,
- (lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(Ixix) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, (Ixx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(Ixxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(IXXV) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger

protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions,

_(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions.

- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of the X11beta complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the X11beta complex selected from
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

- (iv) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- _(v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,

- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions.
- (xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166"

encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

- (xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally-active fragment thereof, or a homolog-thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a

nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and

(xxxiii) "similar to SD27354p [Drosophila melanogaster]" (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster]" encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster]" nucleic acid or its complement under low stringency conditions, wherein

said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% FicoII, 0.2% BSA, 100 ug/mI denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that

hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,

- (iv) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions.
- (vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions.
- (ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2

protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,
- (xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,
- (xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,
- (xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,
- (xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

- (xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions.

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

- 24: A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions,
- (ii) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (iii) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (iv) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (v) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,

- (vii) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (viii) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (ix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (x) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xi) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,
- (xii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,
- (xiii) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,
- (xiv) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xv) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xvi) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of —"Hypothetical-protein FLJ20397" encoded-by-a-nucleic-acid-that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions.

(xviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xix) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,

(xx) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions.

(xxi) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxii) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,

(xxiii) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,

(xxiv) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,

(xxv) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,

(xxvi) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,

(xxvii) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (xxx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(xxxii) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, comprising the steps of

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of (a) exposing said complex, or a cell or organism containing X11beta complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a

gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether
- (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or

- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions, and/or (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes

to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions, and/or

(xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or

- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "Dynein light chain 2A" (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A" encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or

- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or
- (xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions, and/or
- (xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or
- (xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2

protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a" encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or

(xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or (xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a

(xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions, and/or

- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (I) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1"

encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or

- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or
- (Iv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or
- (Ivi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or (Ivii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions, and/or
- (Iviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or

- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or
- (lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or

_(lxvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions, and/or

(lxviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that _hybridizes_to_the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxix) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, and/or (lxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions, and/or (lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, is present in the complex.

- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

- 25. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
 - 36. The method of No. 35, wherein the amount of said complex is determined.
 - 37. The method of No. 35, wherein the activity of said complex is determined.
 - 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
 - 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
 - 40. The method of No. 39, wherein said determining step comprises determining whether (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19" encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its complement under low stringency conditions, and/or
 - (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a

nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions, and/or

- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CGBO_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGBO_HUMAN" encoded by a nucleic acid that hybridizes to the "CGBO_HUMAN" nucleic acid or its complement under low stringency conditions, and/or (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions, and/or (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1" encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions, and/or

- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions, and/or (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A" encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A" nucleic acid or its complement under low stringency conditions, and/or (xvii) "Dynein light chain 2A" (SEQ ID No:39) or a functionally active derivative to the second conditions.

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light

chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions, and/or (xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a

functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions, and/or

(xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and/or (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a"

encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Hypothetical protein FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

- (xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions, and/or
- (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions, and/or
- (xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions, and/or
- (xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions, and/or
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions, and/or

- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions, and/or
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (I) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions, and/or
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions, and/or
- (Iv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions, and/or

- (Ivi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, and/or (Ivii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions, and/or
- (Iviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, and/or

(ixiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions, and/or

(lxv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions, and/or

(Ixvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions, and/or

(Ixviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxix) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, and/or (lxx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions, and/or

(Ixxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions, and/or (lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low

(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, is present in the complex.

stringency conditions, and/or

- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the transactivation of reporter genes by APP-Gal4/VP16 (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins
 (i) "ADAMTS-19" (SEQ ID No:25) or a functionally active derivative thereof, or a
 functionally active fragment thereof, or a homolog thereof, or a variant of "ADAMTS-19"
 encoded by a nucleic acid that hybridizes to the "ADAMTS-19" nucleic acid or its
 complement under low stringency conditions,

- (ii) "APLP1" (SEQ ID No:7) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP1" encoded by a nucleic acid that hybridizes to the "APLP1" nucleic acid or its complement under low stringency conditions,
- (iii) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (iv) "Axonemal dynein heavy chain 8" (SEQ ID No:26) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Axonemal dynein heavy chain 8" encoded by a nucleic acid that hybridizes to the "Axonemal dynein heavy chain 8" nucleic acid or its complement under low stringency conditions,
- (v) "BAT1" (SEQ ID No:27) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BAT1" encoded by a nucleic acid that hybridizes to the "BAT1" nucleic acid or its complement under low stringency conditions,
- (vi) "C20orf11 (sim to a region of RANBPM)" (SEQ ID No:28) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "C20orf11 (sim to a region of RANBPM)" encoded by a nucleic acid that hybridizes to the "C20orf11 (sim to a region of RANBPM)" nucleic acid or its complement under low stringency conditions,
- (vii) "CGB0_HUMAN" (SEQ ID No:29) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGB0_HUMAN" encoded by a nucleic acid that hybridizes to the "CGB0_HUMAN" nucleic acid or its complement under low stringency conditions,
- (viii) "Cadherin EGF LAG seven-pass G-type receptor 2" (SEQ ID No:30) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cadherin EGF LAG seven-pass G-type receptor 2" encoded by a nucleic acid that hybridizes to the "Cadherin EGF LAG seven-pass G-type receptor 2" nucleic acid or its complement under low stringency conditions,
- (ix) "Calsyntenin-1" (SEQ ID No:31) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-1"

- encoded by a nucleic acid that hybridizes to the "Calsyntenin-1" nucleic acid or its complement under low stringency conditions,
- (x) "Calsyntenin-2" (SEQ ID No:32) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-2" encoded by a nucleic acid that hybridizes to the "Calsyntenin-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Calsyntenin-3" (SEQ ID No:33) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calsyntenin-3" encoded by a nucleic acid that hybridizes to the "Calsyntenin-3" nucleic acid or its complement under low stringency conditions,
- (xii) "Chondroitin sulfate proteoglycan 6" (SEQ ID No:34) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chondroitin sulfate proteoglycan 6" encoded by a nucleic acid that hybridizes to the "Chondroitin sulfate proteoglycan 6" nucleic acid or its complement under low stringency conditions,
- (xiii) "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" (SEQ ID No:35) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" encoded by a nucleic acid that hybridizes to the "Chromatin-specific transcription elongation factor FACT 140 kDa subunit" nucleic acid or its complement under low stringency conditions,
- (xiv) "DC6 protein" (SEQ ID No:36) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DC6 protein" encoded by a nucleic acid that hybridizes to the "DC6 protein" nucleic acid or its complement under low stringency conditions,
- (xv) "Dkfzp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dkfzp586c1924" encoded by a nucleic acid that hybridizes to the "Dkfzp586c1924" nucleic acid or its complement under low stringency conditions,
- (xvi) "Dynein light chain 2A " (SEQ ID No:38) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain 2A" encoded by a nucleic acid that hybridizes to the "Dynein light chain 2A" nucleic acid or its complement under low stringency conditions,

(xvii) "Dynein light chain-A" (SEQ ID No:39) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynein light chain-A" encoded by a nucleic acid that hybridizes to the "Dynein light chain-A" nucleic acid or its complement under low stringency conditions,

(xviii) "ELAVL3" (SEQ ID No:40) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ELAVL3" encoded by a nucleic acid that hybridizes to the "ELAVL3" nucleic acid or its complement under low stringency conditions,

- (xix) "ENG00000168820 (hypothetical protein with p-loop)" (SEQ ID No:41) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG00000168820 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ENG00000168820 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions,
- (xx) "Eukaryotic translation initiation factor 4A, isoform" (SEQ ID No:42) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Eukaryotic translation initiation factor 4A, isoform" encoded by a nucleic acid that hybridizes to the "Eukaryotic translation initiation factor 4A, isoform" nucleic acid or its complement under low stringency conditions,
- (xxi) "FLJ13910" (SEQ ID No:43) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13910" encoded by a nucleic acid that hybridizes to the "FLJ13910" nucleic acid or its complement under low stringency conditions,
- (xxii) "FRAP1" (SEQ ID No:44) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FRAP1" encoded by a nucleic acid that hybridizes to the "FRAP1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Filamin, gamma" (SEQ ID No:45) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Filamin, gamma" encoded by a nucleic acid that hybridizes to the "Filamin, gamma" nucleic acid or its complement under low stringency conditions,

(xxiv) "GTP-binding protein ERA" (SEQ ID No:46) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTP-binding protein ERA" encoded by a nucleic acid that hybridizes to the "GTP-binding protein ERA" nucleic acid or its complement under low stringency conditions,

(xxv) "HADH2/ERAB (mitochondrial enzyme)" (SEQ ID No:47) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HADH2/ERAB (mitochondrial enzyme)" encoded by a nucleic acid that hybridizes to the "HADH2/ERAB (mitochondrial enzyme)" nucleic acid or its complement under low stringency conditions,

(xxvi) "HDAC2" (SEQ ID No:48) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HDAC2" encoded by a nucleic acid that hybridizes to the "HDAC2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HERC2 protein" (SEQ ID No:49) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HERC2 protein" encoded by a nucleic acid that hybridizes to the "HERC2 protein" nucleic acid or its complement under low stringency conditions,

(xxviii) "HSPC154" (SEQ ID No:50) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC154" encoded by a nucleic acid that hybridizes to the "HSPC154" nucleic acid or its complement under low stringency conditions,

(xxix) "HSPC245" (SEQ ID No:51) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HSPC245" encoded by a nucleic acid that hybridizes to the "HSPC245" nucleic acid or its complement under low stringency conditions,

(xxx) "HYPOTHETICAL PROTEIN FLJ10618" (SEQ ID No:52) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ10618" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ10618" nucleic acid or its complement under low stringency conditions,

(xxxi) "HYPOTHETICAL PROTEIN FLJ12599" (SEQ ID No:53) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN FLJ12599" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN FLJ12599" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hunc18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hunc18a"

encoded by a nucleic acid that hybridizes to the "Hunc18a" nucleic acid or its complement under low stringency conditions,

_(xxxiii) "Hypothetical protein FLJ10795" (SEQ ID No:55) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ10795" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ10795" nucleic acid or its complement under low stringency conditions,

-(xxxiv)_"Hypothetical_protein_FLJ20397" (SEQ ID No:56) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ20397" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ20397" nucleic acid or its complement under low stringency conditions,

(xxxv) "IKAP" (SEQ ID No:57) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IKAP" encoded by a nucleic acid that hybridizes to the "IKAP" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "KIAA0056" (SEQ ID No:59) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0056" encoded by a nucleic acid that hybridizes to the "KIAA0056" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0166" (SEQ ID No:60) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0166" encoded by a nucleic acid that hybridizes to the "KIAA0166" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0325 (FRAGMENT)" (SEQ ID No:61) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0325 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0325 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xl) "KIAA0564" (SEQ ID No:62) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0564" encoded by a nucleic acid that hybridizes to the "KIAA0564" nucleic acid or its complement under low stringency conditions,
- (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,
- (xlii) "LIB (leucine-rich repeat protein)" (SEQ ID No:64) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LIB (leucine-rich repeat protein)" encoded by a nucleic acid that hybridizes to the "LIB (leucine-rich repeat protein)" nucleic acid or its complement under low stringency conditions,
- (xliii) "Laminin, gamma 1 " (SEQ ID No:65) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Laminin, gamma 1 " encoded by a nucleic acid that hybridizes to the "Laminin, gamma 1 " nucleic acid or its complement under low stringency conditions,
- (xliv) "MBIP" (SEQ ID No:66) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MBIP" encoded by a nucleic acid that hybridizes to the "MBIP" nucleic acid or its complement under low stringency conditions,
- (xiv) "MEGF7 (FRAGMENT)" (SEQ ID No:67) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEGF7 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "MEGF7 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xlvi) "MT-ACT48" (SEQ ID No:68) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MT-ACT48" encoded by a nucleic acid that hybridizes to the "MT-ACT48" nucleic acid or its complement under low stringency conditions,
- (xlvii) "Myosin IXB" (SEQ ID No:69) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Myosin IXB" encoded by a nucleic acid that hybridizes to the "Myosin IXB" nucleic acid or its complement under low stringency conditions,

- (xlviii) "NEU1" (SEQ ID No:70) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NEU1" encoded by a nucleic acid that hybridizes to the "NEU1" nucleic acid or its complement under low stringency conditions,
- (xlix) "NIPSNAP1" (SEQ ID No:71) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP1" encoded by a nucleic acid that hybridizes to the "NIPSNAP1" nucleic acid or its complement under low stringency conditions,
- (I) "NIPSNAP2" (SEQ ID No:72) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NIPSNAP2" encoded by a nucleic acid that hybridizes to the "NIPSNAP2" nucleic acid or its complement under low stringency conditions,
- (li) "Neurexin-1" (SEQ ID No:73) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurexin-1" encoded by a nucleic acid that hybridizes to the "Neurexin-1" nucleic acid or its complement under low stringency conditions,
- (lii) "PDZ and LIM domain protein 1" (SEQ ID No:74) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PDZ and LIM domain protein 1" encoded by a nucleic acid that hybridizes to the "PDZ and LIM domain protein 1" nucleic acid or its complement under low stringency conditions,
- (liii) "PILB" (SEQ ID No:75) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILB" encoded by a nucleic acid that hybridizes to the "PILB" nucleic acid or its complement under low stringency conditions,
- (liv) "PILT" (SEQ ID No:76) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PILT" encoded by a nucleic acid that hybridizes to the "PILT" nucleic acid or its complement under low stringency conditions,
- (Iv) "Paladin" (SEQ ID No:77) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Paladin" encoded by a nucleic acid that hybridizes to the "Paladin" nucleic acid or its complement under low stringency conditions,

(Ivi) "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" (SEQ ID No:78) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" encoded by a nucleic acid that hybridizes to the "Phosphoenolpyruvate carboxykinase 2 (mitochondrial)" nucleic acid or its complement under low stringency conditions, (Ivii) "Procollagen C-endopeptidase enhancer" (SEQ ID No:79) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Procollagen C-endopeptidase enhancer" encoded by a nucleic acid that hybridizes to the "Procollagen C-endopeptidase enhancer" nucleic acid or its complement under low stringency conditions,

(Iviii) "Programmed cell death 10" (SEQ ID No:80) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Programmed cell death 10" encoded by a nucleic acid that hybridizes to the "Programmed cell death 10" nucleic acid or its complement under low stringency conditions,

- (lix) "Protein similar to AGCP6688" (SEQ ID No:81) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to AGCP6688" encoded by a nucleic acid that hybridizes to the "Protein similar to AGCP6688" nucleic acid or its complement under low stringency conditions, (Ix) "RAB7L1" (SEQ ID No:82) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB7L1" encoded by a nucleic acid that hybridizes to the "RAB7L1" nucleic acid or its complement under low stringency conditions,
- (Ixi) "RANBP1" (SEQ ID No:83) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RANBP1" encoded by a nucleic acid that hybridizes to the "RANBP1" nucleic acid or its complement under low stringency conditions,
- (lxii) "RPGR-interacting protein 1" (SEQ ID No:84) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPGR-interacting protein 1" encoded by a nucleic acid that hybridizes to the "RPGR-interacting protein 1" nucleic acid or its complement under low stringency conditions, (lxiii) "Reelin" (SEQ ID No:85) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Reelin" encoded by a

nucleic acid that hybridizes to the "Reelin" nucleic acid or its complement under low stringency conditions,

(Ixiv) "SNAP-25" (SEQ ID No:86) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SNAP-25" encoded by a nucleic acid that hybridizes to the "SNAP-25" nucleic acid or its complement under low stringency conditions,

(Ixv) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxvi) "STX1A" (SEQ ID No:88) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STX1A" encoded by a nucleic acid that hybridizes to the "STX1A" nucleic acid or its complement under low stringency conditions,

(Ixvii) "SUCLA2" (SEQ ID No:89) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SUCLA2" encoded by a nucleic acid that hybridizes to the "SUCLA2" nucleic acid or its complement under low stringency conditions,

(Ixviii) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxix) "Sortilin-related receptor" (SEQ ID No:91) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin-related receptor" encoded by a nucleic acid that hybridizes to the "Sortilin-related receptor" nucleic acid or its complement under low stringency conditions, (Ixx) "Synaptogyrin 3" (SEQ ID No:92) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Synaptogyrin 3" encoded by a nucleic acid that hybridizes to the "Synaptogyrin 3" nucleic acid or its complement under low stringency conditions,

(lxxi) "TYK2" (SEQ ID No:93) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TYK2" encoded by a

nucleic acid that hybridizes to the "TYK2" nucleic acid or its complement under low stringency conditions,

(lxxii) "Ubiquitin-protein ligase E3-alpha" (SEQ ID No:94) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase E3-alpha" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase E3-alpha" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "VGF nerve growth factor inducible protein" (SEQ ID No:95) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "VGF nerve growth factor inducible protein" encoded by a nucleic acid that hybridizes to the "VGF nerve growth factor inducible protein" nucleic acid or its complement under low stringency conditions,

(Ixxiv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

(Ixxv) "Zinc finger protein 198" (SEQ ID No:97) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Zinc finger protein 198" encoded by a nucleic acid that hybridizes to the "Zinc finger protein 198" nucleic acid or its complement under low stringency conditions,

(lxxvi) "hypothetical protein MGC13186" (SEQ ID No:98) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC13186" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC13186" nucleic acid or its complement under low stringency conditions, and/or(lxxvii) "similar to SD27354p [Drosophila melanogaster] " (SEQ ID No:99) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "similar to SD27354p [Drosophila melanogaster] " encoded by a nucleic acid that hybridizes to the "similar to SD27354p [Drosophila melanogaster] " nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis.

The present invention further relates to the following embodiments of the Presenilin-2 complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (ii) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (iii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and
- (iv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,

- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a

nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,

- (xi) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiii) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xiv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (xvi) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,
- (xvii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, (xviii) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein"

encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, (xix) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,

- (xx) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xxi) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,
- (xxii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxiv) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,
- (xxv) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,
- (xxvi) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1"

- encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,
- __(xxvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
 - (xxviii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
 - (xxix) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
 - (xxx) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
 - (xxxi) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,
- (xxxii) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,
- (xxxiii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,
- (xxxiv) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,

(xxxv) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxxix) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

- (xl) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xli) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xliii) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xliv) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlv) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlvii) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,

(xlviii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,

(xlix) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,

- (I) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,
- (ii) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (lii) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (Iiii) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,
- (liv) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,
- (Iv) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (Iviii) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1"

encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,

- (lix) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,
- (Ix) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (Ixii) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,
- (lxiii) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,
- (lxiv) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,
- (lxv) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,
- (lxvi) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(Ixviii) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxix) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxi) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxii) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxiv) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxv) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxvi) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, (lxxviii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxix) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, (lxxx) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxii) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3"

encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and (lxxxiii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 2. The protein complex according to No. 1 wherein the first protein is the protein "Presenilin-2" (SEQ ID NO. 172), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Presenilin-2' encoded by a nucleic acid that hybridizes to the 'Presenilin-2' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,

- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions.
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,
- (xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions,

- (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,
- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,
- (xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions.
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that

hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2"

encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (I) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,
- (ii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,
- (lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (Iv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,
- (Iviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4"

encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,

- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (ix) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,
- (Ixvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(Ixvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin"

encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(Ixxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, (lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, (lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions.

- 4. The protein complex according to No. 1 comprising all but 1 82 of the following proteins:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200

kDa proteasome activator" nucleic acid or its complement under low stringency conditions,

- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions.
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,

- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,
- (xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,
- (xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,
- (xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090"

encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions.

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin"

encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (I) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,
- (ii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,
- (Iii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (Iv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,

- (Iviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (Ix) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (Ixi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (Ixii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,
- (Ixiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (Ixiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (Ixv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,
- (lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6"

encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(Ixviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions,

(Ixix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(Ixxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(Ixxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(Ixxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, (lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded

by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, (lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(Ixxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, (lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions.

5. The complex of any of No. 1 - 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.

- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.

- 12. Component of the Presentiin 2 complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the Presenilin 2 complex selected from
- (i) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555"

encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,
- (xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,
- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

- ---(xvi)."KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its —complement-under low stringency conditions,
 - (xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
 - (xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
 - (xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,
 - (xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,
 - (xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,
 - (xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a

nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% FicoII, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or

functionally active derivatives thereof_selected_from_the second group of proteins according to No. 1 (b).

- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,

- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,
- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,

- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,
- (xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions.
- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,

(xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

- 24. 'A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (iv) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (v) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (vii) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420"

encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

- (viii) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,
- (ix) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,
- (x) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,
- (xiii) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions.
- (xiv) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

- (xv) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,
- (xvi) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,
- (xvii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xviii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xix) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,
- (xx) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions,
- (xxi) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,
- (xxii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform

1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(xxiii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, comprising the steps of

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 - 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Presenilin 2 complex to one or more candidate molecules; and

- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.

- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1"

encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions, and/or

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- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic

acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions, and/or (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3" encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "ECSIT" (SEQ ID No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1"

encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions, and/or

- (xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or
- (xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

- (xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" —encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement –under low stringency-conditions; and/or
 - (xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions, and/or
 - (xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions, and/or
 - (xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex" encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, and/or (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
 - (I) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or
 - (li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions, and/or

- (lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or
- (Iv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or...
- (Ivi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or
- (Ivii) "PSMB3" (SEQ ID No:155)-or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or
- (Iviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a

- -nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or
 - (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or
 - (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or
 - (Ixiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or
 - (Ixiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or
 - (Ixv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5" encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or
 - (Ixvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or
 - (Ixvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or
 - (lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or

(Ixix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low-stringency conditions, and/or

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or

(Ixxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, and/or (lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes

to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxv) "Wolframin" (SEQ-ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, is present in the complex.

- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or

disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 - 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200

kDa proteasome activator" nucleic acid or its complement under low stringency conditions, and/or

- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the

- "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions, and/or
- (x)-"Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment-thereof, or-a homolog-thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3" encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions, and/or

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, and/or

- (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "Cerebral-protein 10" (SEQ-ID No:120) or a functionally-active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions, and/or
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof; or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions, and/or (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3"

encoded by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "Down syndrome critical_region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii)-"ECSIT"-(SEQ ID No:125) or a-functionally-active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-

glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions, and/or

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions, and/or

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex"

encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, and/or (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

- (I) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions, and/or
- (li) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions, and/or
- (Iv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions, and/or
- (Ivi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions, and/or

- (Ivii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions, and/or
- (Iviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions, and/or
- (lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions, and/or
- (lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5"

encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions, and/or

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions, and/or

(Ixvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions, and/or

(Ixviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions, and/or

(Ixix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions, and/or

(Ixx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions, and/or

(Ixxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions, and/or

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions, and/or

(Ixxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions, and/or

(lxxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions, and/or

(Ixxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoA desaturase" nucleic acid or its complement under low stringency conditions, and/or (lxxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, is present in the complex.

- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins
 (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

- (ii) "200 kDa proteasome activator" (SEQ ID No:101) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "200 kDa proteasome activator" encoded by a nucleic acid that hybridizes to the "200 kDa proteasome activator" nucleic acid or its complement under low stringency conditions,
- (iii) "ABCB11" (SEQ ID No:102) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCB11" encoded by a nucleic acid that hybridizes to the "ABCB11" nucleic acid or its complement under low stringency conditions,
- (iv) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (v) "ATP-binding cassette protein, sub-family B, member 1" (SEQ ID No:104) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette protein, sub-family B, member 1" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette protein, sub-family B, member 1" nucleic acid or its complement under low stringency conditions, (vi) "ATP-dependent metalloprotease FtsH1 homolog" (SEQ ID No:105) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-dependent metalloprotease FtsH1 homolog" encoded by a nucleic acid that hybridizes to the "ATP-dependent metalloprotease FtsH1 homolog" nucleic acid or its complement under low stringency conditions,
- (vii) "ATP7A" (SEQ ID No:106) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP7A" encoded by a nucleic acid that hybridizes to the "ATP7A" nucleic acid or its complement under low stringency conditions,
- (viii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (ix) "Adrenoleukodystrophy protein" (SEQ ID No:108) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

- "Adrenoleukodystrophy protein" encoded by a nucleic acid that hybridizes to the "Adrenoleukodystrophy protein" nucleic acid or its complement under low stringency conditions,
- (x) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xi) "BIG1" (SEQ ID No:110) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BIG1" encoded by a nucleic acid that hybridizes to the "BIG1" nucleic acid or its complement under low stringency conditions,
- (xii) "BTAF1" (SEQ ID No:111) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BTAF1" encoded by a nucleic acid that hybridizes to the "BTAF1" nucleic acid or its complement under low stringency conditions,
- (xiii) "CD97" (SEQ ID No:112) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CD97" encoded by a nucleic acid that hybridizes to the "CD97" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDM_HUMAN" (SEQ ID No:113) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDM_HUMAN" encoded by a nucleic acid that hybridizes to the "CDM_HUMAN" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CGI-51" (SEQ ID No:115) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-51" encoded by a nucleic acid that hybridizes to the "CGI-51" nucleic acid or its complement under low stringency conditions,
- (xvii) "CHRNA3" (SEQ ID No:116) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CHRNA3"

encoded by a nucleic acid that hybridizes to the "CHRNA3" nucleic acid or its complement under low stringency conditions,

(xviii) "Calcium-binding protein P22" (SEQ ID No:117) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Calcium-binding protein P22" encoded by a nucleic acid that hybridizes to the "Calcium-binding protein P22" nucleic acid or its complement under low stringency conditions, (xix) "Cation-chloride cotransporter-interacting protein" (SEQ ID No:118) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cation-chloride cotransporter-interacting protein" encoded by a nucleic acid that hybridizes to the "Cation-chloride cotransporter-interacting protein" nucleic acid or its complement under low stringency conditions,

- (xx) "Centromere/kinetochore protein ZW10 homolog" (SEQ ID No:119) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Centromere/kinetochore protein ZW10 homolog" encoded by a nucleic acid that hybridizes to the "Centromere/kinetochore protein ZW10 homolog" nucleic acid or its complement under low stringency conditions,
- (xxi) "Cerebral protein 10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein 10" encoded by a nucleic acid that hybridizes to the "Cerebral protein 10" nucleic acid or its complement under low stringency conditions,
- (xxii) "DAAM1" (SEQ ID No:121) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAAM1" encoded by a nucleic acid that hybridizes to the "DAAM1" nucleic acid or its complement under low stringency conditions,
- (xxiii) "DAPK1" (SEQ ID No:122) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DAPK1" encoded by a nucleic acid that hybridizes to the "DAPK1" nucleic acid or its complement under low stringency conditions,
- (xxiv) "DKFZp586c1924" (SEQ ID No:37) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DKFZp586c1924" encoded by a nucleic acid that hybridizes to the "DKFZp586c1924" nucleic acid or its complement under low stringency conditions,
- (xxv) "DOCK3" (SEQ ID No:123) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DOCK3"

encoded-by a nucleic acid that hybridizes to the "DOCK3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Down syndrome critical region protein 2" (SEQ ID No:124) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Down syndrome critical region protein 2" encoded by a nucleic acid that hybridizes to the "Down syndrome critical region protein 2" nucleic acid or its complement under low stringency conditions,

(xxvii) "ECSIT" (SEQ-ID-No:125) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ECSIT" encoded by a nucleic acid that hybridizes to the "ECSIT" nucleic acid or its complement under low stringency conditions,

(xxviii) "FACL1" (SEQ ID No:126) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL1" encoded by a nucleic acid that hybridizes to the "FACL1" nucleic acid or its complement under low stringency conditions,

(xxix) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xxx) "FLJ20420" (SEQ ID No:128) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20420" encoded by a nucleic acid that hybridizes to the "FLJ20420" nucleic acid or its complement under low stringency conditions,

(xxxi) "FLJ22555" (SEQ ID No:129) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22555" encoded by a nucleic acid that hybridizes to the "FLJ22555" nucleic acid or its complement under low stringency conditions,

(xxxii) "FLJ22678" (SEQ ID No:130) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22678" encoded by a nucleic acid that hybridizes to the "FLJ22678" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" (SEQ ID No:131) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Galactosylgalactosylxylosylprotein 3-beta-

glucuronosyltransferase 3" encoded by a nucleic acid that hybridizes to the "Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase 3" nucleic acid or its complement under low stringency conditions,

(xxxiv) "HTRA2" (SEQ ID No:132) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HTRA2" encoded by a nucleic acid that hybridizes to the "HTRA2" nucleic acid or its complement under low stringency conditions,

(xxxv) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxxvi) "HYPOTHETICAL PROTEIN XP_174405" (SEQ ID No:134) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN XP_174405" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN XP_174405" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Hypothetical protein FLJ23356" (SEQ ID No:135) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23356" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23356" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Hypothetical protein KIAA0455" (SEQ ID No:136) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0455" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0455" nucleic acid or its complement under low stringency conditions,

(xxxix) "Hypothetical protein KIAA0971-I" (SEQ ID No:137) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0971-I" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0971-I" nucleic acid or its complement under low stringency conditions,

(xl) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0090" (SEQ ID No:139) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0090" encoded by a nucleic acid that hybridizes to the "KIAA0090" nucleic acid or its complement under low stringency conditions,

(xlii) "KIAA0103" (SEQ ID No:140) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0103" encoded by a nucleic acid that hybridizes to the "KIAA0103" nucleic acid or its complement under low stringency conditions,

(xliii) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xliv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,

(xlv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xlvi) "NPC1" (SEQ ID No:144) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPC1" encoded by a nucleic acid that hybridizes to the "NPC1" nucleic acid or its complement under low stringency conditions,

(xlvii) "NPD002" (SEQ ID No:145) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPD002" encoded by a nucleic acid that hybridizes to the "NPD002" nucleic acid or its complement under low stringency conditions,

(xlviii) "NPL4, a component of the nuclear pore complex" (SEQ ID No:146) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NPL4, a component of the nuclear pore complex"

encoded by a nucleic acid that hybridizes to the "NPL4, a component of the nuclear pore complex" nucleic acid or its complement under low stringency conditions, (xlix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions.

- (I) "P63 protein" (SEQ ID No:148) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "P63 protein" encoded by a nucleic acid that hybridizes to the "P63 protein" nucleic acid or its complement under low stringency conditions,
- (Ii) "PSMA1" (SEQ ID No:149) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA1" encoded by a nucleic acid that hybridizes to the "PSMA1" nucleic acid or its complement under low stringency conditions,
- (iii) "PSMA3" (SEQ ID No:150) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA3" encoded by a nucleic acid that hybridizes to the "PSMA3" nucleic acid or its complement under low stringency conditions,
- (liii) "PSMA4" (SEQ ID No:151) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA4" encoded by a nucleic acid that hybridizes to the "PSMA4" nucleic acid or its complement under low stringency conditions,
- (liv) "PSMA6" (SEQ ID No:152) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMA6" encoded by a nucleic acid that hybridizes to the "PSMA6" nucleic acid or its complement under low stringency conditions,
- (Iv) "PSMB1" (SEQ ID No:153) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB1" encoded by a nucleic acid that hybridizes to the "PSMB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PSMB2" (SEQ ID No:154) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB2" encoded by a nucleic acid that hybridizes to the "PSMB2" nucleic acid or its complement under low stringency conditions,

- (Ivii) "PSMB3" (SEQ ID No:155) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB3" encoded by a nucleic acid that hybridizes to the "PSMB3" nucleic acid or its complement under low stringency conditions,
- (Iviii) "PSMB4" (SEQ ID No:156) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB4" encoded by a nucleic acid that hybridizes to the "PSMB4" nucleic acid or its complement under low stringency conditions,
- (lix) "PSMB5" (SEQ ID No:157) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB5" encoded by a nucleic acid that hybridizes to the "PSMB5" nucleic acid or its complement under low stringency conditions,
- (Ix) "PSMB6" (SEQ ID No:158) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMB6" encoded by a nucleic acid that hybridizes to the "PSMB6" nucleic acid or its complement under low stringency conditions,
- (lxi) "PSMC1" (SEQ ID No:159) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC1" encoded by a nucleic acid that hybridizes to the "PSMC1" nucleic acid or its complement under low stringency conditions,
- (lxii) "PSMC2" (SEQ ID No:160) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC2" encoded by a nucleic acid that hybridizes to the "PSMC2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "PSMC3" (SEQ ID No:161) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC3" encoded by a nucleic acid that hybridizes to the "PSMC3" nucleic acid or its complement under low stringency conditions,
- (Ixiv) "PSMC4" (SEQ ID No:162) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC4" encoded by a nucleic acid that hybridizes to the "PSMC4" nucleic acid or its complement under low stringency conditions,
- (lxv) "PSMC5" (SEQ ID No:163) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC5"

encoded by a nucleic acid that hybridizes to the "PSMC5" nucleic acid or its complement under low stringency conditions,

(lxvi) "PSMC6" (SEQ ID No:164) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMC6" encoded by a nucleic acid that hybridizes to the "PSMC6" nucleic acid or its complement under low stringency conditions,

(lxvii) "PSMD1" (SEQ ID No:165) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD1" encoded by a nucleic acid that hybridizes to the "PSMD1" nucleic acid or its complement under low stringency conditions,

(lxviii) "PSMD11" (SEQ ID No:166) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD11" encoded by a nucleic acid that hybridizes to the "PSMD11" nucleic acid or its complement under low stringency conditions.

(lxix) "PSMD12" (SEQ ID No:167) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD12" encoded by a nucleic acid that hybridizes to the "PSMD12" nucleic acid or its complement under low stringency conditions,

(lxx) "PSMD13" (SEQ ID No:168) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD13" encoded by a nucleic acid that hybridizes to the "PSMD13" nucleic acid or its complement under low stringency conditions,

(lxxi) "PSMD2" (SEQ ID No:169) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD2" encoded by a nucleic acid that hybridizes to the "PSMD2" nucleic acid or its complement under low stringency conditions,

(lxxii) "PSMD3" (SEQ ID No:170) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD3" encoded by a nucleic acid that hybridizes to the "PSMD3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "PSMD4" (SEQ ID No:171) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PSMD4" encoded by a nucleic acid that hybridizes to the "PSMD4" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,

(lxxv) "Prohibitin" (SEQ ID No:173) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Prohibitin" encoded by a nucleic acid that hybridizes to the "Prohibitin" nucleic acid or its complement under low stringency conditions,

(lxxvi) "RPS6KA3" (SEQ ID No:174) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RPS6KA3" encoded by a nucleic acid that hybridizes to the "RPS6KA3" nucleic acid or its complement under low stringency conditions,

(lxxvii) "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" (SEQ ID No:175) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" encoded by a nucleic acid that hybridizes to the "SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10" nucleic acid or its complement under low stringency conditions,

(Ixxviii) "STRA6 isoform 1" (SEQ ID No:176) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STRA6 isoform 1" encoded by a nucleic acid that hybridizes to the "STRA6 isoform 1" nucleic acid or its complement under low stringency conditions,

(lxxix) "Serine/threonine protein phosphatase 6" (SEQ ID No:90) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Serine/threonine protein phosphatase 6" encoded by a nucleic acid that hybridizes to the "Serine/threonine protein phosphatase 6" nucleic acid or its complement under low stringency conditions,

(lxxx) "Sortilin 1" (SEQ ID No:177) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sortilin 1" encoded by a nucleic acid that hybridizes to the "Sortilin 1" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Stearoyl-CoA desaturase" (SEQ ID No:178) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Stearoyl-CoA desaturase" encoded by a nucleic acid that hybridizes to the "Stearoyl-CoArdesaturase" nucleic acid or its complement under low stringency conditions, (Ixxxii) "Tparl" (SEQ ID No:179) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tparl" encoded by a nucleic acid that hybridizes to the "Tparl" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "Ubiquitin-protein ligase EDD" (SEQ ID No:180) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Ubiquitin-protein ligase EDD" encoded by a nucleic acid that hybridizes to the "Ubiquitin-protein ligase EDD" nucleic acid or its complement under low stringency conditions, (lxxxiv) "Voltage-dependent anion channel 2" (SEQ ID No:181) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Voltage-dependent anion channel 2" encoded by a nucleic acid that hybridizes to the "Voltage-dependent anion channel 2" nucleic acid or its complement under low stringency conditions,

(lxxxv) "Wolframin" (SEQ ID No:182) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Wolframin" encoded by a nucleic acid that hybridizes to the "Wolframin" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "cholinergic receptor, nicotinic, alpha polypeptide 3" (SEQ ID No:183) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "cholinergic receptor, nicotinic, alpha polypeptide 3" encoded by a nucleic acid that hybridizes to the "cholinergic receptor, nicotinic, alpha polypeptide 3" nucleic acid or its complement under low stringency conditions, and/or(lxxxvii) "ensp00000297280 (hypothetical protein with p-loop)" (SEQ ID No:184) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ensp00000297280 (hypothetical protein with p-loop)" encoded by a nucleic acid that hybridizes to the "ensp00000297280 (hypothetical protein with p-loop)" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Nicastrincomplex:

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (ii) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (iii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (iv) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (v) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and
- (vi) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid

that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (v) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,
- (vi) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (vii) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions, (viii) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (ix) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a

nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

- (x) "Delta-6 fatty acid desaturase" (SEQ.ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, (xi) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active-fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (xii) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
 - (xiii) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
 - (xiv) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
 - (xv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
 - (xvi) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
 - (xvii) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

- (xviii) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,
- (xix) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (xx) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (xxi) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxii) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxiii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,
- (xxiv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions.
- (xxv) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxvi) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, (xxvii) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xxviii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxix) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxi) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2"

encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xxxv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xxxvi) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and

(xxxvii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

2. The protein complex according to No. 1 wherein the first protein is the protein 'Nicastrin' (SEQ ID NO. 147), or a functionally active derivative thereof, or a functionally

active fragment thereof, or a homolog thereof, or a variant of 'Nicastrin' encoded by a nucleic acid that hybridizes to the 'Nicastrin' under low stringency conditions.

- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant-of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4"

encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions.
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,

(xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,

(xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

(xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, (xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1"

encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a homolog thereof, or a variant of "REP8 protein"

functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency

conditions,

- (xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,
- (xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or
- (xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions,
- and a protein complex selected from complex (II) and comprising the following proteins: (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- -(v)-"BSCv-protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (vi) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,
 - (vii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
 - (viii) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions, (ix) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
 - (x) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
 - (xi) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, (xii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (xiii) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,

- (xiv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xv) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (xix) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xx) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxi) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxiii) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxiv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxv) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvi) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxvii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxviii) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, (xxix) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xxx) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxi) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, (xxxv) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a

functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein"

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encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxvii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, (xxxvii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xxxix) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xl) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or

(xli) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions.

- 4. The protein complex according to No. 1 comprising all but 1 36 of the following proteins:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof; or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,

- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase-II beta chain"-nucleic acid or its complement under low stringency conditions,
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977"

encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,

(xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,

(xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,

(xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" -encoded-by-a-nucleic-acid that-hybridizes-to-the-"NICE-3"-nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, (xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions,

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions.

(xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,

(xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions,

(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions.

- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

- 8. The complex of any of No. 1 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of the Nicastrin complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the Nicastrin complex selected from
- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic

acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions,
- (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, (xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and (xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoli, 0.2% BSA, 100 ug/ml denatured

- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25

mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions.
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions.
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390"

encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
 - (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
 - (x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
 - (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions,
 - (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,
 - (xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
 - (xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that

hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,
- (ii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (iii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (iv) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions.
- (v) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (vi) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390"

encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

- (vii) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (x) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,
- (xi) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof,
- or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions,
- (xiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that

hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, comprising the steps of

- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Nicastrin complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.

- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that-hybridizes-to the-"18-kDa-microsomal-signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4"

encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions, and/or

- (xv) "FACL4" (SEQ ID No.196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

- (xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions, and/or
- (xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or
- (xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament

for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.

- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (v) "BACE1" (SEQ ID No:187) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a

nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions, and/or

- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions, and/or
- (xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2"

encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, and/or (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain

- dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or
- (xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes -to-the-"Stromal-cell-derived-factor-2-like-1"-nucleic-acid-or-its complement under low stringency conditions, and/or
- (xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or
- (xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or
- (xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions,is present in the complex.
- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of,

the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins), or protein components of, said complex.

- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iii) "ATP-binding cassette, sub-family A, member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof,

or a variant of "ATP-binding cassette, sub-family A, member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A, member 3" nucleic acid or its complement under low stringency conditions,

- (iv) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (v)-"BACE1" (SEQ-ID-No:187)-or-a-functionally-active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BACE1" encoded by a nucleic acid that hybridizes to the "BACE1" nucleic acid or its complement under low stringency conditions,
- (vi) "BSCv protein (FRAGMENT)" (SEQ ID No:188) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "BSCv protein (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "BSCv protein (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (vii) "CAMK4" (SEQ ID No:189) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK4" encoded by a nucleic acid that hybridizes to the "CAMK4" nucleic acid or its complement under low stringency conditions,
- (viii) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (ix) "Casein kinase II beta chain" (SEQ ID No:190) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Casein kinase II beta chain" encoded by a nucleic acid that hybridizes to the "Casein kinase II beta chain" nucleic acid or its complement under low stringency conditions,
- (x) "Cathepsin B" (SEQ ID No:191) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cathepsin B" encoded by a nucleic acid that hybridizes to the "Cathepsin B" nucleic acid or its complement under low stringency conditions,
- (xi) "DCTN1" (SEQ ID No:192) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DCTN1" encoded by a

nucleic acid that hybridizes to the "DCTN1" nucleic acid or its complement under low stringency conditions,

- (xii) "Delta-6 fatty acid desaturase" (SEQ ID No:193) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-6 fatty acid desaturase" encoded by a nucleic acid that hybridizes to the "Delta-6 fatty acid desaturase" nucleic acid or its complement under low stringency conditions, (xiii) "ENSG00000144840" (SEQ ID No:194) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENSG00000144840" encoded by a nucleic acid that hybridizes to the "ENSG00000144840" nucleic acid or its complement under low stringency conditions, (xiv) "FACL3" (SEQ ID No:195) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL3" encoded by a nucleic acid that hybridizes to the "FACL3" nucleic acid or its complement under low stringency conditions,
- (xv) "FACL4" (SEQ ID No:196) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FACL4" encoded by a nucleic acid that hybridizes to the "FACL4" nucleic acid or its complement under low stringency conditions,
- (xvi) "FLJ13977" (SEQ ID No:197) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13977" encoded by a nucleic acid that hybridizes to the "FLJ13977" nucleic acid or its complement under low stringency conditions,
- (xvii) "FLJ20342" (SEQ ID No:127) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20342" encoded by a nucleic acid that hybridizes to the "FLJ20342" nucleic acid or its complement under low stringency conditions,
- (xviii) "FLJ20481" (SEQ ID No:198) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ20481" encoded by a nucleic acid that hybridizes to the "FLJ20481" nucleic acid or its complement under low stringency conditions,
- (xix) "FLJ22390" (SEQ ID No:199) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ22390" encoded by a nucleic acid that hybridizes to the "FLJ22390" nucleic acid or its complement under low stringency conditions,

(xx) "ICAM-2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM-2" encoded by a nucleic acid that hybridizes to the "ICAM-2" nucleic acid or its complement under low stringency conditions,

(xxi) "KIAA0095" (SEQ ID No:201) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0095" encoded by a nucleic acid that hybridizes to the "KIAA0095" nucleic acid or its complement under low stringency conditions,

(xxii) "KIAA0922" (SEQ ID No:202) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0922" encoded by a nucleic acid that hybridizes to the "KIAA0922" nucleic acid or its complement under low stringency conditions,

(xxiii) "KIAA1181 (FRAGMENT)" (SEQ ID No:203) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1181 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1181 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxiv) "KIAA1533 (FRAGMENT)" (SEQ ID No:204) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1533 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA1533 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxv) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxvi) "NICE-3" (SEQ ID No:143) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NICE-3" encoded by a nucleic acid that hybridizes to the "NICE-3" nucleic acid or its complement under low stringency conditions,

(xxvii) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(xxviii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

(xxix) "PAS domain containing serine/threonine kinase" (SEQ ID No:207) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PAS domain containing serine/threonine kinase" encoded by a nucleic acid that hybridizes to the "PAS domain containing serine/threonine kinase" nucleic acid or its complement under low stringency conditions, (xxx) "PP1, regulatory subunit 15B" (SEQ ID No:208) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP1, regulatory subunit 15B" encoded by a nucleic acid that hybridizes to the "PP1, regulatory subunit 15B" nucleic acid or its complement under low stringency conditions, (xxxi) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Presenilin-1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-1" encoded by a nucleic acid that hybridizes to the "Presenilin-1" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Presenilin-2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin-2" encoded by a nucleic acid that hybridizes to the "Presenilin-2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Protein amplified in osteosarcoma (OS-9)" (SEQ ID No:211) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein amplified in osteosarcoma (OS-9)" encoded by a nucleic acid that hybridizes to the "Protein amplified in osteosarcoma (OS-9)" nucleic acid or its complement under low stringency conditions,

(xxxv) "Protein similar to stromal cell-derived factor 2" (SEQ ID No:212) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protein similar to stromal cell-derived factor 2" encoded by a nucleic acid

that hybridizes to the "Protein similar to stromal cell-derived factor 2" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, (xxxvii) "REP8 protein" (SEQ ID No:214) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REP8 protein" encoded by a nucleic acid that hybridizes to the "REP8 protein" nucleic acid or its

complement under low stringency conditions, (xxxviii) "RING finger protein 5" (SEQ ID No:215) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RING finger protein 5" encoded by a nucleic acid that hybridizes to the "RING finger protein 5" nucleic acid or its complement under low stringency conditions, (xxxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

- (xl) "Stromal cell-derived factor 2-like 1" (SEQ ID No:217) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Stromal cell-derived factor 2-like 1" encoded by a nucleic acid that hybridizes to the "Stromal cell-derived factor 2-like 1" nucleic acid or its complement under low stringency conditions,
- (xli) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,
- (xlii) "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" (SEQ ID No:219) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)" encoded by a nucleic acid that hybridizes to the "homolog

of yeast golgi membrane protein yif1p (yip1p-interacting factor)" nucleic acid or its complement under low stringency conditions, and/or(xliii) "tyrosine phosphatase ensg00000149185" (SEQ ID No:220) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tyrosine phosphatase ensg00000149185" encoded by a nucleic acid that hybridizes to the "tyrosine phosphatase ensg00000149185" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Aph1a-complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (iii) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (iv) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
- (v) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2"

encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and

- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "18 kDa microsomal signal peptidase subunit" (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a

nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,

- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xiv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (xv) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (xvii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xviii) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xix) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xx) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions.

(xxiii) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxiv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxv) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvi) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxvii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxviii) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions.

(xxix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiii) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxiv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxv) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxviii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xxxix) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xl) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

- (xiii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,
- (xliii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,
- (xliv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,
- (xlv) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,
- (xlvi) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlvii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

_(xlviii) "Neurotrypsin" (SEQ_ID_No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

- (xlix) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (I) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6"

encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

- (Iv) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (Ivii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (Iviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (Ixii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,

(lxiii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, (lxiv) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixv) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(lxvi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(Ixvii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixviii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxix) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, (lxx) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (Ixxi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, (lxxiii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, (lxxv) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(Ixxvi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions.

(Ixxvii) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxviii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxix) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(Ixxx) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and (lxxxii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% FicoIl, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a

buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 2. The protein complex according to No. 1 wherein the first protein is the protein 'Aph1a' (SEQ ID NO. 109), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Aph1a' encoded by a nucleic acid that hybridizes to the 'Aph1a' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency_conditions, _____
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes

to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic-receptor Endo180" nucleic acid or its complement under low stringency conditions.

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions.

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions.

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions.

(xxix) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

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variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xiv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a

nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlvi) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions.

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions.
- (I) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes

to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (Iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (Iviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (Ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,

- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, (lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain

dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency

(IXX) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a —functionally-active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, (lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(Ixxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, (Ixxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(Ixxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, (Ixxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(Ixxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(Ixxxii) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(Ixxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins: (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,

- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,

- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions.

- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,

- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions.
- (xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,
- (xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

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(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xivi) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

(I) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (ii) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (Iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (Iviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,

- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" rencoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (Ixi) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (Ixii) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions.
- (Ixiv) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (Ixv) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (Ixvi) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(Ixvii) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixviii) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(Ixix) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(lxx) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxxi) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(Ixxii) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, (Ixxiii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (Ixxiv) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic

acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxv) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, (lxxvi) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, (lxxviii) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxix) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxx) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxi) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(Ixxxii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(ixxxiii) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (lxxxv) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions.

- 4. The protein complex according to No. 1 comprising all but 1 81 of the following proteins:
- (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that

hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions,

- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1"

encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,

- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1"

encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,

- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,
- (xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,
- (xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,
- (xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,
- (xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic

acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions.

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to

the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ-ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active-fragment-thereof, or a homolog-thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xI) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xIi) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xivi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions.

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin"

encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,

- (I) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (ii) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (Iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB"

encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,

- (Iviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (Ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (Ixii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (Ixiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions.

(lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,

(Ixvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,

(lxviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, (lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1"

encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, (lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, (lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, (lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(Ixxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(Ixxxii) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(Ixxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(Ixxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(Ixxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, (lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes

to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions.

- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is

attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.

- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- __11._The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
 - 12. Component of the Aph-1a complex obtainable by a process according to any of No. 9 11.
 - 13. Protein of the Aph-1a complex selected from
 - (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
 - (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
 - (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
 - (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
 - (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,
- (ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions;
- (x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions.
- (xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions. (xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions. (xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xix) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that

hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions.

(xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions.

(xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin

7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency

conditions,

(xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP

synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- The kit according to No. 18 for processing a substrate of said complex.

- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a

nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,

- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,
- (viii) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions,
- (ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,
- (x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,
- (xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the

"Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xix) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that

hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

(xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin

7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, (xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin

beta 8" nucleic acid or its complement under low stringency conditions, (xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions.

(xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions.

(xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP

synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(xxxvi) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID-No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(xxxix) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (ii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (iii) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (v) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (vi) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions,
- (vii) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

- (viii) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions.
- (ix) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions.
- (x) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions.
- (xi) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,
- (xii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,
- (xiii) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xiv) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions,

(xv) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xvi) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xvii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xviii) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xix) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions.

(xx) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions.

(xxi) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,

(xxii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions.

(xxiii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,

(xxiv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,

(xxv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,

(xxvi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,

(xxvii) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,

(xxviii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,

(xxix) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,

(xxx) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,

(xxxi) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(xxxii) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (xxxiii) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, (xxxiv) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement

(xxxv) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

under low stringency conditions,

(xxxvi) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(xxxvii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(xxxviii) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

- -(xxxix) "integral membrane transporter protein" (SEQ ID-No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
 - (xl) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, comprising the steps of
 - (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
 - (b) determinig whether said candidate molecule is bound to the complex or protein.
 - 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Aph-1a complex to one or more candidate molecules; and
 - (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription

level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.

- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions, and/or
- - (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
 - (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or
 - (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions, and/or
 - (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions, and/or
 - (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions, and/or
 - (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or

- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions, and/or

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(xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions, and/or

(xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions, and/or

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions, and/or

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN" nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xi) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions, and/or

(xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or

(I) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or

- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions, and/or
- (Ivi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions, and/or
- (Ivii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions, and/or
- (Iviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or

- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions, and/or
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (lxi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (lxii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (ixiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions, and/or
- (lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, and/or (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or
- (Ixvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL"

encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions, and/or

(Ixviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, and/or (Ixix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(Ixxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions, and/or

(lxxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, and/or

(Ixxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, and/or (Ixxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(Ixxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, and/or (Ixxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(Ixxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, and/or

(Ixxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions, and/or

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(lxxxii) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions, and/or (lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions, and/or (lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions, and/or (lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, is present in the complex.

32. The method of any of No. 26 - 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions, and/or
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a

nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions, and/or

- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions, and/or

- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions, and/or
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions, and/or
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions, and/or (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions, and/or
- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions, and/or
- (xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions, and/or
- (xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions, and/or

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions, and/or

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions, and/or

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions, and/or

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions, and/or

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions, and/or

(xxix) "HYPOTHETICAL PROTEIN " (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN " encoded by a nucleic acid that hybridizes to the "HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions, and/or

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions, and/or

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions, and/or

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions, and/or

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions, and/or

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions, and/or

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions, and/or

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions, and/or

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions, and/or

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, and/or (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions, and/or

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions, and/or

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions, and/or

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions, and/or

(xlvi) "MGC4248 " (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248 "

encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions, and/or

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions, and/or

(xiviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions, and/or

- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions, and/or
- (I) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions, and/or
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions, and/or
- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions, and/or
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4"

encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions, and/or

- (Iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions, and/or
- (Ivi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions, and/or
- (Ivii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions, and/or
- (Iviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions, and/or
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions, and/or
- (Ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (Ixi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (Ixii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or

(lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions, and/or

(lxiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions, and/or (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions, and/or (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions, and/or

(lxvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions, and/or

(Ixviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions, and/or (Ixix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions, and/or

(lxx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B".

encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions, and/or

(lixi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions, and/or

(Ixxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions, and/or

(lxxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions, and/or

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, and/or (lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, and/or (lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, and/or (lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

-variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions, and/or

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF-interacting)" nucleic acid or its complement under low stringency conditions, and/or

(lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions, and/or

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions, and/or

(lxxxii) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions, and/or (lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions, and/or

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions, and/or

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by-a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or

(Ixxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or (Ixxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, is present in the complex.

- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of

RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins (i) "18 kDa microsomal signal peptidase subunit " (SEQ ID No:100) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "18 kDa microsomal signal peptidase subunit " encoded by a nucleic acid that hybridizes to the "18 kDa microsomal signal peptidase subunit " nucleic acid or its complement under low stringency conditions,
- (ii) "23 kDa microsomal signal peptidase" (SEQ ID No:221) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "23 kDa microsomal signal peptidase" encoded by a nucleic acid that hybridizes to the "23 kDa microsomal signal peptidase" nucleic acid or its complement under low stringency conditions.
- (iii) "25 kDa microsomal signal peptidase subunit" (SEQ ID No:185) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "25 kDa microsomal signal peptidase subunit" encoded by a nucleic acid that hybridizes to the "25 kDa microsomal signal peptidase subunit" nucleic acid or its complement under low stringency conditions,
- (iv) "ABCC1" (SEQ ID No:222) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ABCC1" encoded by a nucleic acid that hybridizes to the "ABCC1" nucleic acid or its complement under low stringency conditions,
- (v) "APLP2" (SEQ ID No:8) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APLP2" encoded by a

nucleic acid that hybridizes to the "APLP2" nucleic acid or its complement under low stringency conditions,

- (vi) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (vii) "ATM" (SEQ ID No:103) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATM" encoded by a nucleic acid that hybridizes to the "ATM" nucleic acid or its complement under low stringency conditions,
- (viii) "ATP-binding cassette, sub-family A member 3" (SEQ ID No:186) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP-binding cassette, sub-family A member 3" encoded by a nucleic acid that hybridizes to the "ATP-binding cassette, sub-family A member 3" nucleic acid or its complement under low stringency conditions,
- (ix) "ATP1B1" (SEQ ID No:223) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP1B1" encoded by a nucleic acid that hybridizes to the "ATP1B1" nucleic acid or its complement under low stringency conditions,
- (x) "ATP2C1" (SEQ ID No:224) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ATP2C1" encoded by a nucleic acid that hybridizes to the "ATP2C1" nucleic acid or its complement under low stringency conditions,
- (xi) "Acetolactate synthase homolog" (SEQ ID No:107) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Acetolactate synthase homolog" encoded by a nucleic acid that hybridizes to the "Acetolactate synthase homolog" nucleic acid or its complement under low stringency conditions,
- (xii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (xiii) "Brain-specific GTP-binding protein" (SEQ ID No:225) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a

variant of "Brain-specific GTP-binding protein" encoded by a nucleic acid that hybridizes to the "Brain-specific GTP-binding protein" nucleic acid or its complement under low stringency conditions,

- (xiv) "CDW92" (SEQ ID No:226) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CDW92" encoded by a nucleic acid that hybridizes to the "CDW92" nucleic acid or its complement under low stringency conditions,
- (xv) "CGI-13" (SEQ ID No:114) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CGI-13" encoded by a nucleic acid that hybridizes to the "CGI-13" nucleic acid or its complement under low stringency conditions,
- (xvi) "CNTNAP1" (SEQ ID No:227) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CNTNAP1" encoded by a nucleic acid that hybridizes to the "CNTNAP1" nucleic acid or its complement under low stringency conditions,
- (xvii) "Cerebral protein-10" (SEQ ID No:120) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Cerebral protein-10" encoded by a nucleic acid that hybridizes to the "Cerebral protein-10" nucleic acid or its complement under low stringency conditions.
- (xviii) "DNM1" (SEQ ID No:228) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "DNM1" encoded by a nucleic acid that hybridizes to the "DNM1" nucleic acid or its complement under low stringency conditions,
- (xix) "Dihydrofolate reductase" (SEQ ID No:229) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dihydrofolate reductase" encoded by a nucleic acid that hybridizes to the "Dihydrofolate reductase" nucleic acid or its complement under low stringency conditions,
- (xx) "ENG" (SEQ ID No:230) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ENG" encoded by a nucleic acid that hybridizes to the "ENG" nucleic acid or its complement under low stringency conditions,
- (xxi) "EXT2" (SEQ ID No:231) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXT2" encoded by a

nucleic acid that hybridizes to the "EXT2" nucleic acid or its complement under low stringency conditions,

(xxii) "EXTL3" (SEQ ID No:232) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "EXTL3" encoded by a nucleic acid that hybridizes to the "EXTL3" nucleic acid or its complement under low stringency conditions,

(xxiii) "Endocytic receptor Endo180" (SEQ ID No:233) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Endocytic receptor Endo180" encoded by a nucleic acid that hybridizes to the "Endocytic receptor Endo180" nucleic acid or its complement under low stringency conditions,

(xxiv) "FLJ13660" (SEQ ID No:234) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ13660" encoded by a nucleic acid that hybridizes to the "FLJ13660" nucleic acid or its complement under low stringency conditions,

(xxv) "GPR49" (SEQ ID No:235) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GPR49" encoded by a nucleic acid that hybridizes to the "GPR49" nucleic acid or its complement under low stringency conditions,

(xxvi) "HK2" (SEQ ID No:236) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HK2" encoded by a nucleic acid that hybridizes to the "HK2" nucleic acid or its complement under low stringency conditions,

(xxvii) "HU-K4" (SEQ ID No:133) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HU-K4" encoded by a nucleic acid that hybridizes to the "HU-K4" nucleic acid or its complement under low stringency conditions,

(xxviii) "HUNC18a" (SEQ ID No:54) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HUNC18a" encoded by a nucleic acid that hybridizes to the "HUNC18a" nucleic acid or its complement under low stringency conditions,

(xxix) "HYPOTHETICAL PROTEIN" (SEQ ID No:237) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "HYPOTHETICAL PROTEIN" encoded by a nucleic acid that hybridizes to the

"HYPOTHETICAL PROTEIN " nucleic acid or its complement under low stringency conditions,

(xxx) "Hypothetical protein (Fragment)" (SEQ ID No:238) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein (Fragment)" encoded by a nucleic acid that hybridizes to the "Hypothetical protein (Fragment)" nucleic acid or its complement under low stringency conditions,

(xxxi) "Hypothetical protein FLJ14562" (SEQ ID No:239) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ14562" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ14562" nucleic acid or its complement under low stringency conditions,

(xxxii) "Hypothetical protein FLJ23630" (SEQ ID No:240) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein FLJ23630" encoded by a nucleic acid that hybridizes to the "Hypothetical protein FLJ23630" nucleic acid or its complement under low stringency conditions,

(xxxiii) "Hypothetical protein KIAA0372" (SEQ ID No:241) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Hypothetical protein KIAA0372" encoded by a nucleic acid that hybridizes to the "Hypothetical protein KIAA0372" nucleic acid or its complement under low stringency conditions,

(xxxiv) "ICAM2" (SEQ ID No:200) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ICAM2" encoded by a nucleic acid that hybridizes to the "ICAM2" nucleic acid or its complement under low stringency conditions,

(xxxv) "IGF2R" (SEQ ID No:242) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IGF2R" encoded by a nucleic acid that hybridizes to the "IGF2R" nucleic acid or its complement under low stringency conditions,

(xxxvi) "ITPR1" (SEQ ID No:243) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ITPR1" encoded by a nucleic acid that hybridizes to the "ITPR1" nucleic acid or its complement under low stringency conditions,

(xxxvii) "Insulinoma-glucagonoma protein 20" (SEQ ID No:58) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Insulinoma-glucagonoma protein 20" encoded by a nucleic acid that hybridizes to the "Insulinoma-glucagonoma protein 20" nucleic acid or its complement under low stringency conditions,

(xxxviii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane-protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,

(xxxix) "KIAA0062 (FRAGMENT)" (SEQ ID No:138) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0062 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0062 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xl) "KIAA0251 (FRAGMENT)" (SEQ ID No:244) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0251 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0251 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xli) "KIAA0363 (FRAGMENT)" (SEQ ID No:245) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0363 (FRAGMENT)" encoded by a nucleic acid that hybridizes to the "KIAA0363 (FRAGMENT)" nucleic acid or its complement under low stringency conditions, (xlii) "KIAA0763" (SEQ ID No:63) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0763" encoded by a nucleic acid that hybridizes to the "KIAA0763" nucleic acid or its complement under low stringency conditions,

(xliii) "KIAA0971" (SEQ ID No:246) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA0971" encoded by a nucleic acid that hybridizes to the "KIAA0971" nucleic acid or its complement under low stringency conditions,

(xliv) "KIAA1250" (SEQ ID No:247) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1250" encoded by a nucleic acid that hybridizes to the "KIAA1250" nucleic acid or its complement under low stringency conditions,

(xlv) "LRP5" (SEQ ID No:248) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "LRP5" encoded by a nucleic acid that hybridizes to the "LRP5" nucleic acid or its complement under low stringency conditions,

(xlvi) "MGC4248" (SEQ ID No:141) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4248" encoded by a nucleic acid that hybridizes to the "MGC4248" nucleic acid or its complement under low stringency conditions,

(xlvii) "Mesenchymal stem cell protein DSCD75" (SEQ ID No:205) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Mesenchymal stem cell protein DSCD75" encoded by a nucleic acid that hybridizes to the "Mesenchymal stem cell protein DSCD75" nucleic acid or its complement under low stringency conditions,

(xlviii) "NRP2" (SEQ ID No:249) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NRP2" encoded by a nucleic acid that hybridizes to the "NRP2" nucleic acid or its complement under low stringency conditions,

- (xlix) "Neurotrypsin" (SEQ ID No:206) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurotrypsin" encoded by a nucleic acid that hybridizes to the "Neurotrypsin" nucleic acid or its complement under low stringency conditions,
- (I) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (li) "PCDHA10" (SEQ ID No:250) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHA10" encoded by a nucleic acid that hybridizes to the "PCDHA10" nucleic acid or its complement under low stringency conditions,
- (lii) "PCDHB12" (SEQ ID No:251) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB12" encoded by a nucleic acid that hybridizes to the "PCDHB12" nucleic acid or its complement under low stringency conditions,

- (liii) "PCDHB13: protocadherin beta 13" (SEQ ID No:252) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB13: protocadherin beta 13" encoded by a nucleic acid that hybridizes to the "PCDHB13: protocadherin beta 13" nucleic acid or its complement under low stringency conditions,
- (liv) "PCDHB4" (SEQ ID No:253) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHB4" encoded by a nucleic acid that hybridizes to the "PCDHB4" nucleic acid or its complement under low stringency conditions,
- (Iv) "PCDHGB1" (SEQ ID No:254) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB1" encoded by a nucleic acid that hybridizes to the "PCDHGB1" nucleic acid or its complement under low stringency conditions,
- (Ivi) "PCDHGB6" (SEQ ID No:255) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PCDHGB6" encoded by a nucleic acid that hybridizes to the "PCDHGB6" nucleic acid or its complement under low stringency conditions,
- (Ivii) "PMPCB" (SEQ ID No:256) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PMPCB" encoded by a nucleic acid that hybridizes to the "PMPCB" nucleic acid or its complement under low stringency conditions,
- (Iviii) "PP2C gamma" (SEQ ID No:257) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PP2C gamma" encoded by a nucleic acid that hybridizes to the "PP2C gamma" nucleic acid or its complement under low stringency conditions,
- (lix) "Pcdhb17" (SEQ ID No:258) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pcdhb17" encoded by a nucleic acid that hybridizes to the "Pcdhb17" nucleic acid or its complement under low stringency conditions,
- (lx) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (|xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (Ixii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (lxiii) "Protocadherin 7" (SEQ ID No:259) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin 7" encoded by a nucleic acid that hybridizes to the "Protocadherin 7" nucleic acid or its complement under low stringency conditions,
- (ixiv) "Protocadherin beta 16" (SEQ ID No:260) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 16" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 16" nucleic acid or its complement under low stringency conditions,
- (lxv) "Protocadherin beta 8" (SEQ ID No:213) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Protocadherin beta 8" encoded by a nucleic acid that hybridizes to the "Protocadherin beta 8" nucleic acid or its complement under low stringency conditions,
- (lxvi) "RAB-18" (SEQ ID No:261) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RAB-18" encoded by a nucleic acid that hybridizes to the "RAB-18" nucleic acid or its complement under low stringency conditions,
- (Ixvii) "RNASEL" (SEQ ID No:262) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "RNASEL" encoded by a nucleic acid that hybridizes to the "RNASEL" nucleic acid or its complement under low stringency conditions,
- (Ixviii) "Rab3 GTPase-activating protein, non-catalytic subunit" (SEQ ID No:263) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Rab3 GTPase-activating protein, non-catalytic subunit" encoded by a nucleic acid that hybridizes to the "Rab3 GTPase-activating protein, non-catalytic subunit" nucleic acid or its complement under low stringency conditions,

(lxix) "Retinal short-chain dehydrogenase/reductase retSDR2" (SEQ ID No:216) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Retinal short-chain dehydrogenase/reductase retSDR2" encoded by a nucleic acid that hybridizes to the "Retinal short-chain dehydrogenase/reductase retSDR2" nucleic acid or its complement under low stringency conditions,

(Ixx) "SMAP-1B" (SEQ ID No:264) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SMAP-1B" encoded by a nucleic acid that hybridizes to the "SMAP-1B" nucleic acid or its complement under low stringency conditions,

(lxxi) "SPTLC2" (SEQ ID No:265) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "SPTLC2" encoded by a nucleic acid that hybridizes to the "SPTLC2" nucleic acid or its complement under low stringency conditions,

(Ixxii) "STMN3" (SEQ ID No:87) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "STMN3" encoded by a nucleic acid that hybridizes to the "STMN3" nucleic acid or its complement under low stringency conditions,

(Ixxiii) "Sideroflexin 1" (SEQ ID No:266) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sideroflexin 1" encoded by a nucleic acid that hybridizes to the "Sideroflexin 1" nucleic acid or its complement under low stringency conditions,

(lxxiv) "Signal transducer and activator of transcription-1" (SEQ ID No:267) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Signal transducer and activator of transcription-1" encoded by a nucleic acid that hybridizes to the "Signal transducer and activator of transcription-1" nucleic acid or its complement under low stringency conditions, (lxxv) "Similar to CGI-135 protein" (SEQ ID No:268) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Similar to CGI-135 protein" encoded by a nucleic acid that hybridizes to the "Similar to CGI-135 protein" nucleic acid or its complement under low stringency conditions, (lxxvi) "Sterile alpha and HEAT/Armadillo motif protein" (SEQ ID No:269) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterile alpha and HEAT/Armadillo motif protein" encoded by a nucleic

acid that hybridizes to the "Sterile alpha and HEAT/Armadillo motif protein" nucleic acid or its complement under low stringency conditions,

(lxxvii) "Sterol O-acyltransferase 1" (SEQ ID No:270) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Sterol O-acyltransferase 1" encoded by a nucleic acid that hybridizes to the "Sterol O-acyltransferase 1" nucleic acid or its complement under low stringency conditions, (lxxviii) "Thioredoxin domain-containing protein" (SEQ ID No:218) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Thioredoxin domain-containing protein" encoded by a nucleic acid that hybridizes to the "Thioredoxin domain-containing protein" nucleic acid or its complement under low stringency conditions,

(lxxix) "Triple functional domain protein (PTPRF interacting)" (SEQ ID No:271) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Triple functional domain protein (PTPRF interacting)" encoded by a nucleic acid that hybridizes to the "Triple functional domain protein (PTPRF interacting)" nucleic acid or its complement under low stringency conditions, (lxxx) "UNC5C" (SEQ ID No:272) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "UNC5C" encoded by a nucleic acid that hybridizes to the "UNC5C" nucleic acid or its complement under low stringency conditions,

(lxxxi) "Vacuolar ATP synthase membrane sector associated protein m8-9" (SEQ ID No:273) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Vacuolar ATP synthase membrane sector associated protein m8-9" encoded by a nucleic acid that hybridizes to the "Vacuolar ATP synthase membrane sector associated protein m8-9" nucleic acid or its complement under low stringency conditions,

(lxxxii) "Y391_HUMAN" (SEQ ID No:274) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Y391_HUMAN" encoded by a nucleic acid that hybridizes to the "Y391_HUMAN" nucleic acid or its complement under low stringency conditions,

(lxxxiii) "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" (SEQ ID No:275) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" encoded by a nucleic acid that hybridizes to the

"hypothetical protein MGC10924 similar to Nedd4 WW-binding protein 5" nucleic acid or its complement under low stringency conditions,

(lxxxiv) "hypothetical protein MGC22916" (SEQ ID No:276) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "hypothetical protein MGC22916" encoded by a nucleic acid that hybridizes to the "hypothetical protein MGC22916" nucleic acid or its complement under low stringency conditions,

(lxxxv) "integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

(lxxxvi) "tegt: testis enhanced gene transcript (bax inhibitor 1)" (SEQ ID No:278) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "tegt: testis enhanced gene transcript (bax inhibitor 1)" encoded by a nucleic acid that hybridizes to the "tegt: testis enhanced gene transcript (bax inhibitor 1)" nucleic acid or its complement under low stringency conditions, and/or(lxxxvii) "vacuolar protein sorting protein 18" (SEQ ID No:279) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "vacuolar protein sorting protein 18" encoded by a nucleic acid that hybridizes to the "vacuolar protein sorting protein 18" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the Pen-2.complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

- (ii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (iii) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and
- (iv) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, (iii) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a
- functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1

catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,

- (vi) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions.
- (vii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (ix) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (x) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and
- (xi) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% FicoII, 0.2% BSA, 100 ug/mI denatured salmon sperm DNA, and 10% (wt/voI) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

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- 2. The protein complex according to No. 1 wherein the first protein is the protein 'Pen-2' (SEQ ID NO. 209), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Pen-2' encoded by a nucleic acid that hybridizes to the 'Pen-2' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102"

(Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions.
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions,

- and a protein complex selected from complex (II) and comprising the following proteins:

 (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a

 functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2

 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid

 or its complement under low stringency conditions,
- (ii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER"-encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iii) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (iv) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (v) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (viii) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,

- (ix) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (x) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xi) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiii) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.
- 4. The protein complex according to No. 1 comprising all but 1 10 of the following proteins:
- (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a

nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,

- (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,
- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,

- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a hornolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions,
- (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions.
- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 ~ 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.

- 8. The complex of any of No. 1 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
 - 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
 - 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
 - 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
 - 12. Component of the Pen-2 complex obtainable by a process according to any of No. 9 11.
 - 13. Protein of the Pen-2 complex selected from
 - (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of

"COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and
- (iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 60 Celsius.
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).

- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic-acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:

- (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)"
- nucleic acid or its complement under low stringency conditions,

 (iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or

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- (iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, (ii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,

- (iii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that_hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under-low-stringency-conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Pen-2 complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.

- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid
- or its complement under low stringency conditions, and/or
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1

catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or

- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

- (xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.

37. The method of No. 35, wherein the activity of said complex is determined.

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- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803" encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions, and/or
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1"

encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or

(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions is present in the complex.

- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of. the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.

- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins (i) "Alpha-2 catenin" (SEQ ID No:280) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha-2 catenin" encoded by a nucleic acid that hybridizes to the "Alpha-2 catenin" nucleic acid or its complement under low stringency conditions,
- (ii) "Aph-1a" (SEQ ID No:109) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Aph-1a" encoded by a nucleic acid that hybridizes to the "Aph-1a" nucleic acid or its complement under low stringency conditions,
- (iii) "COPINE FAMILY MEMBER" (SEQ ID No:281) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "COPINE FAMILY MEMBER" encoded by a nucleic acid that hybridizes to the "COPINE FAMILY MEMBER" nucleic acid or its complement under low stringency conditions,
- (iv) "Copine III" (SEQ ID No:282) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Copine III" encoded by a nucleic acid that hybridizes to the "Copine III" nucleic acid or its complement under low stringency conditions,
- (v) "Dachshund 2" (SEQ ID No:283) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dachshund 2" encoded by a nucleic acid that hybridizes to the "Dachshund 2" nucleic acid or its complement under low stringency conditions,
- (vi) "Delta-1 catenin" (SEQ ID No:284) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-1 catenin" encoded by a nucleic acid that hybridizes to the "Delta-1 catenin" nucleic acid or its complement under low stringency conditions,
- (vii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (viii) "MGC2803" (SEQ ID No:286) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC2803"

encoded by a nucleic acid that hybridizes to the "MGC2803" nucleic acid or its complement under low stringency conditions,

- (ix) "Nicastrin" (SEQ ID No:147) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nicastrin" encoded by a nucleic acid that hybridizes to the "Nicastrin" nucleic acid or its complement under low stringency conditions,
- (x) "Pen-2" (SEQ ID No:209) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Pen-2" encoded by a nucleic acid that hybridizes to the "Pen-2" nucleic acid or its complement under low stringency conditions,
- (xi) "Presenilin 1" (SEQ ID No:210) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 1" encoded by a nucleic acid that hybridizes to the "Presenilin 1" nucleic acid or its complement under low stringency conditions,
- (xii) "Presenilin 2" (SEQ ID No:172) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Presenilin 2" encoded by a nucleic acid that hybridizes to the "Presenilin 2" nucleic acid or its complement under low stringency conditions,
- (xiii) "TNRC15" (SEQ ID No:287) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TNRC15" encoded by a nucleic acid that hybridizes to the "TNRC15" nucleic acid or its complement under low stringency conditions,
- (xiv) "TPST1" (SEQ ID No:288) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "TPST1" encoded by a nucleic acid that hybridizes to the "TPST1" nucleic acid or its complement under low stringency conditions, and/or(xv) "ZIP kinase" (SEQ ID No:289) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "ZIP kinase" encoded by a nucleic acid that hybridizes to the "ZIP kinase" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the APP695SW-complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
 - (iv) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and
 - (v) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
 - (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (ii) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a

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nucleic acid that hybridizes to the "GTF21" nucleic acid or its complement under low stringency conditions,

- (iii) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (iv) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (v) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and
- (vi) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
- 2. The protein complex according to No. 1 wherein the first protein is the protein 'APP695SW' (SEQ ID NO. 290), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'APP695SW' encoded by a nucleic acid that hybridizes to the 'APP695SW' under low stringency conditions.

- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:
- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that

hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "GTF21" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF21" encoded by a

nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,

- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (ix) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (x) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.
- 4. The protein complex according to No. 1 comprising all but 1 5 of the following proteins:
- (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions,
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773"

- encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog-thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "GTF21" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF21" encoded by a nucleic acid that hybridizes to the "GTF21" nucleic acid or its complement under low stringency conditions,
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha"

encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.
- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of the APP695SW complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the APP695SW complex selected from
- (i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
 - 14. Nucleic acid encoding a protein according to No. 13.
 - 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or

- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8

comprising the steps of(a) exposing said complex, or a cell or organism containing APP695SW complex to one or more candidate molecules; and

- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (v) "GTF21" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF21" encoded by a nucleic acid that hybridizes to the "GTF21" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or

- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not

having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW" encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773" encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions, and/or
- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as

neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 - 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.
 - 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
 - 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
 - 45. Complex of any of No. 1 8 and/or protein selected from the following proteins
 (i) "APP695SW" (SEQ ID No:290) or a functionally active derivative thereof, or a
 functionally active fragment thereof, or a homolog thereof, or a variant of "APP695SW"
 encoded by a nucleic acid that hybridizes to the "APP695SW" nucleic acid or its
 complement under low stringency conditions,
 - (ii) "FLJ10773" (SEQ ID No:291) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "FLJ10773"

encoded by a nucleic acid that hybridizes to the "FLJ10773" nucleic acid or its complement under low stringency conditions,

- (iii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iv) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (v) "GTF2I" (SEQ ID No:293) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "GTF2I" encoded by a nucleic acid that hybridizes to the "GTF2I" nucleic acid or its complement under low stringency conditions,
- (vi) "IL13RA2" (SEQ ID No:294) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "IL13RA2" encoded by a nucleic acid that hybridizes to the "IL13RA2" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane protein 2B (ITM2B)" (SEQ ID No:16) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane protein 2B (ITM2B)" encoded by a nucleic acid that hybridizes to the "Integral membrane protein 2B (ITM2B)" nucleic acid or its complement under low stringency conditions,
- (viii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (ix) "JIP-1" (SEQ ID No:295) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "JIP-1" encoded by a nucleic acid that hybridizes to the "JIP-1" nucleic acid or its complement under low stringency conditions,
- (x) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha"

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encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or(xi) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The present invention further relates to the following embodiments of the APP-C99-complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (ii) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (iii) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and
- (iv) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid

that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,

- (ii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions.
- (iii) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (iv) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (v) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (vi) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (vii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions.
- (viii) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (ix) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1

related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,

- (x) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xi) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a —functionally-active-fragment-thereof,-or-a-homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xii) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and
- (xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
- 2. The protein complex according to No. 1 wherein the first protein is the protein APP-C99 (SEQ ID NO. 10), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'APP-C99' encoded by a nucleic acid that hybridizes to the 'APP-C99' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions.

- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta"

encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions,

and a protein complex selected from complex (II) and comprising the following proteins:

- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102"

- (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

- 4. The protein complex according to No. 1 comprising all but 1 12 of the following proteins:
- (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions,
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,
- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that

hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,

- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,

(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions.

- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by

modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).

- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of the APP-C99 complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the APP-C99 complex selected from
- (i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and
- (iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442"

encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.

- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and

an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.

- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022"

encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or

- (iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.
- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions.
- (ii) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (iii) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.

- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of (a) exposing said complex, or a cell or organism containing APP-C99 complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.
- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid

that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or

- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949"

encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or

- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "NAP-1" related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or
- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.

- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated

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complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.

- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions, and/or
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions, and/or
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions, and/or

- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions, and/or
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions, and/or
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions, and/or
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions, and/or

- (xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions, and/or (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a
- (xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the production of Abeta-40 and Abeta-42 peptides by ELISA (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the production of C-terminal APP fragments in cell lines or transgenic animals by western blot (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), the proteolytic activity of beta- or gamma secretases towards bacterially expressed APP fragments in vitro (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or transactivation of a Gal4-driven reporter gene (e.g. by modifying the expression of one or several interacting

proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins
 (i) "APP" (SEQ ID No:9) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP" encoded by a nucleic acid that hybridizes to the "APP" nucleic acid or its complement under low stringency conditions.
- (ii) "APP-C99" (SEQ ID No:10) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "APP-C99" encoded by a nucleic acid that hybridizes to the "APP-C99" nucleic acid or its complement under low stringency conditions,
- (iii) "CAMK2D" (SEQ ID No:297) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "CAMK2D" encoded by a nucleic acid that hybridizes to the "CAMK2D" nucleic acid or its complement under low stringency conditions,
- (iv) "Delta-like homolog" (SEQ ID No:298) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Delta-like homolog" encoded by a nucleic acid that hybridizes to the "Delta-like homolog" nucleic acid or its complement under low stringency conditions,
- (v) "Fe65" (SEQ ID No:13) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65" encoded by a nucleic acid that hybridizes to the "Fe65" nucleic acid or its complement under low stringency conditions,
- (vi) "Fe65L1" (SEQ ID No:292) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Fe65L1" encoded by a nucleic acid that hybridizes to the "Fe65L1" nucleic acid or its complement under low stringency conditions,

- (vii) "Integral membrane transporter protein" (SEQ ID No:277) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Integral membrane transporter protein" encoded by a nucleic acid that hybridizes to the "Integral membrane transporter protein" nucleic acid or its complement under low stringency conditions,
- (viii) "KIAA1102 (Fragment)" (SEQ ID No:285) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1102 (Fragment)" encoded by a nucleic acid that hybridizes to the "KIAA1102 (Fragment)" nucleic acid or its complement under low stringency conditions,
- (ix) "KIAA1949" (SEQ ID No:299) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "KIAA1949" encoded by a nucleic acid that hybridizes to the "KIAA1949" nucleic acid or its complement under low stringency conditions,
- (x) "MGC4022" (SEQ ID No:300) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC4022" encoded by a nucleic acid that hybridizes to the "MGC4022" nucleic acid or its complement under low stringency conditions,
- (xi) "MGC5442" (SEQ ID No:142) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MGC5442" encoded by a nucleic acid that hybridizes to the "MGC5442" nucleic acid or its complement under low stringency conditions,
- (xii) "NAP-1 related protein" (SEQ ID No:301) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "NAP-1 related protein" encoded by a nucleic acid that hybridizes to the "NAP-1 related protein" nucleic acid or its complement under low stringency conditions,
- (xiii) "Neurocalcin delta" (SEQ ID No:302) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Neurocalcin delta" encoded by a nucleic acid that hybridizes to the "Neurocalcin delta" nucleic acid or its complement under low stringency conditions,
- (xiv) "REST corepressor" (SEQ ID No:303) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "REST corepressor" encoded by a nucleic acid that hybridizes to the "REST corepressor" nucleic acid or its complement under low stringency conditions,

(xv) "S-100 alpha" (SEQ ID No:296) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 alpha" encoded by a nucleic acid that hybridizes to the "S-100 alpha" nucleic acid or its complement under low stringency conditions,

(xvi) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or(xvii) "X11beta" (SEQ ID No:96) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "X11beta" encoded by a nucleic acid that hybridizes to the "X11beta" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

The invention further relates to the following embodiments of the Tau-complex

- 1. A protein complex selected from complex (I) and comprising
- (a) at least one first protein selected from the group consisting of:
- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin"

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encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,

- (v) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
- (vi) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,
- (vii) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, (viii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and
- (ix) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, and
- (b) at least one second protein, which second protein is selected from the group consisting of:
- (i) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions.

- (ii) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (iii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (iv) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and
- (v) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and a complex (II) comprising at least two of said second proteins, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
- 2. The protein complex according to No. 1 wherein the first protein is the protein Tau (SEQ ID NO. 315), or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of 'Tau' encoded by a nucleic acid that hybridizes to the 'Tau' under low stringency conditions.
- 3. The protein complex according to No. 1 selected from complex (I) and comprising the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-

repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,
- (xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.
- 4. The protein complex according to No. 1 comprising all but 1 4 of the following proteins:

- (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-

repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,

- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,
- (xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions,
- (xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions.

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- 5. The complex of any of No. 1 4 comprising a functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein, respectively.
- 6. The complex of No. 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of No. 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of No. 1 7 that is involved in the the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)).
- 9. A process for preparing a complex of any of No. 1 8 and optionally the components thereof comprising the following steps:expressing a protein (bait) of the complex, preferably a tagged protein, in a target cell, isolating the protein complex which is attached to the bait protein, and optionally dissociating the protein complex and isolating the individual complex members.
- 10. The process according to No. 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of No. 9 10 wherein the two tags are separated by a cleavage site for a protease.

- 12. Component of the Tau complex obtainable by a process according to any of No. 9 11.
- 13. Protein of the Tau complex selected from
- (i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCI (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40 Celsius, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1 % SDS for 1.5 hours at 55 Celsius, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60 Celsius.
- 14. Nucleic acid encoding a protein according to No. 13.
- 15. Construct, preferably a vector construct, comprising (a) a nucleic acid according to No. 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
- (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative of at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the first group of proteins according to No. 1 (a) and at least one of said proteins, or functionally active fragments or functionally active derivative thereof being selected from the second group of proteins according to No. 1 (b).
- 16. Host cell, containing a vector comprising at least one of the nucleic acid of No. 14 and/or a construct of No. 15 or containing several vectors each comprising at least the nucleic acid sequence encoding at least one of the proteins, or functionally active fragments or functionally active derivatives thereof selected from the first group of proteins according to No. 1 (a) and the proteins, or functionally active fragments or

functionally active derivatives thereof selected from the second group of proteins according to No. 1 (b).

- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of No. 1 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody which binds to any of the proteins according to No. 13.
- 18. A kit comprising in one or more container the complex of any of No. 1 8 and/or the proteins of No. 13 optionally together with an antibody according to No. 17 and/or further components such as reagents and working instructions.
- 19. The kit according to No. 18 for processing a substrate of said complex.
- 20. The kit according to No. 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 21. Array, in which at least a complex according to any of No. 1 8 and/or at least one protein according to No. 14 and/or at least one antibody according to No. 17 is attached to a solid carrier.
- 22. A process for processing a physiological substrate of the complex comprising the step of bringing into contact a complex to any of No. 1 8 with said substrate, such that said substrate is processed.
- 23. A pharmaceutical composition comprising the protein complex of any of No. 1 8 and/or any of the following the proteins:
- (i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and a pharmaceutical acceptable carrier.

- 24. A pharmaceutical composition according to No. 23 for the treatment of diseases and disorders such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 25. A method for screening for a molecule that binds to the complex of anyone of No. 1 8 and/or any of the following the proteins:
- (i) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, comprising the steps of
- (a) exposing said complex, or a cell or organism containing same to one or more candidate molecules; and
- (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of the complex of any one of No. 1 8 comprising the steps of(a) exposing said complex, or a cell or organism containing Tau complex to one or more candidate molecules; and
- (b) determining the amount of activity of protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity or composition of said complex.
- 27. The method of No. 26, wherein the amount of said complex is determined.

- 28. The method of No. 26, wherein the activity of said complex is determined.
- 29. The method of No. 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of No. 26, wherein the amount of the individual protein components of said complex are determined.
- 31. The method of No. 30, wherein said determining step comprises determining whether (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions, and/or
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions, and/or

- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions, and/or
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or
- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA

regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

- (xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 32. The method of any of No. 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of No. 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of any of No. 1 8 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.
- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, activity of, or component composition of, or intracellular localization of the complex of any one of the No. 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene dependent on the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity,

or protein components of, said complex in an analogous sample from a subject not having the disease or disorder or predisposition indicates the presence in the subject of the disease or disorder or predisposition in the subject.

- 36. The method of No. 35, wherein the amount of said complex is determined.
- 37. The method of No. 35, wherein the activity of said complex is determined.
- 38. The method of No. 37, wherein said determining step comprises isolating from the subject said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of No. 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of No. 39, wherein said determining step comprises determining whether (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions, and/or (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions. and/or
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions, and/or
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin"

encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions, and/or

- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions, and/or
- -(vi)-"Dynactin 2" (SEQ-ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions, and/or
 - (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions, and/or
 - (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions, and/or
 - (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions, and/or
 - (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions, and/or
 - (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)"

encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, and/or (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions, and/or

- (xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or
- (xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, is present in the complex.
- 41. The complex of any one of No. 1 8, or proteins of No. 13 or the antibody or fragment of No. 17, for use in a method of diagnosing a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.
- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity or component composition of or intracellular localization of, the complex of anyone of No. 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, the phosphorylation of tau proteins in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)) or the aggregation of tau proteins into filaments or tangles in vitro or in cells (e.g. by modifying the expression of one or several interacting proteins in cells by means of RNAi (siRNA) and/or plasmids encoding the interacting protein(s)), or protein components of, said complex.

- 43. The method according to No. 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to No. 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of any of No. 1 8 and/or protein selected from the following proteins
 (i) "14-3-3 protein zeta/delta" (SEQ ID No:6) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "14-3-3 protein zeta/delta" encoded by a nucleic acid that hybridizes to the "14-3-3 protein zeta/delta" nucleic acid or its complement under low stringency conditions,
- (ii) "Actin" (SEQ ID No:305) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Actin" encoded by a nucleic acid that hybridizes to the "Actin" nucleic acid or its complement under low stringency conditions,
- (iii) "Alpha tubulin" (SEQ ID No:306) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Alpha tubulin" encoded by a nucleic acid that hybridizes to the "Alpha tubulin" nucleic acid or its complement under low stringency conditions,
- (iv) "Beta tubulin" (SEQ ID No:307) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Beta tubulin" encoded by a nucleic acid that hybridizes to the "Beta tubulin" nucleic acid or its complement under low stringency conditions,
- (v) "Deoxyhypusine synthase" (SEQ ID No:308) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Deoxyhypusine synthase" encoded by a nucleic acid that hybridizes to the "Deoxyhypusine synthase" nucleic acid or its complement under low stringency conditions,
- (vi) "Dynactin 2" (SEQ ID No:309) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Dynactin 2" encoded by a nucleic acid that hybridizes to the "Dynactin 2" nucleic acid or its complement under low stringency conditions,
- (vii) "MEP50" (SEQ ID No:310) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "MEP50" encoded by a

nucleic acid that hybridizes to the "MEP50" nucleic acid or its complement under low stringency conditions,

- (viii) "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" (SEQ ID No:311) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" encoded by a nucleic acid that hybridizes to the "Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1" nucleic acid or its complement under low stringency conditions,
- (ix) "PPP2CA (PP2A, catalytic subunit, alpha)" (SEQ ID No:312) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CA (PP2A, catalytic subunit, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2CA (PP2A, catalytic subunit, alpha)" nucleic acid or its complement under low stringency conditions,
- (x) "PPP2CB (PP2A, catalytic subunit, beta)" (SEQ ID No:313) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2CB (PP2A, catalytic subunit, beta)" encoded by a nucleic acid that hybridizes to the "PPP2CB (PP2A, catalytic subunit, beta)" nucleic acid or its complement under low stringency conditions,
- (xi) "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" (SEQ ID No:314) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)" nucleic acid or its complement under low stringency conditions, (xii) "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" (SEQ ID No:19) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" encoded by a nucleic acid that hybridizes to the "PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)" nucleic acid or its complement under low stringency conditions,
- (xiii) "S-100 beta" (SEQ ID No:304) or a functionally active derivative thereof, or a functionally active fragment thereof, or a homolog thereof, or a variant of "S-100 beta" encoded by a nucleic acid that hybridizes to the "S-100 beta" nucleic acid or its complement under low stringency conditions, and/or(xiv) "Tau" (SEQ ID No:315) or a functionally active derivative thereof, or a functionally active fragment thereof, or a

homolog thereof, or a variant of "Tau" encoded by a nucleic acid that hybridizes to the "Tau" nucleic acid or its complement under low stringency conditions, as a target for an active agent of a pharmaceutical, preferably a drug target in the treatment or prevention of a disease or disorder such as neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders.

5. PROTOCOLS:

The TAP-technology, which is more fully described in EP 1 105 508 B1 and in Rigaut, et al., 1999, Nature Biotechnol. 17:1030-1032 respectively was used and further adapted as described below for protein purification. Proteins were identified using mass spectrometry as described further below.

5.1 Construction of TAP-tagged bait

The cDNAs encoding the complete ORF were obtained by RT-PCR. Total RNA was prepared from appropriate cell lines using the RNeasy Mini Kit (Qiagen). Both cDNA synthesis and PCR were performed with the SUPERSCRIPT One-Step RT-PCR for Long templates Kit (Life Technologies) using gene-specific primers. After 35-40 cycles of amplification PCR-products with the expected size were gel-purified with the MinElute PCR Purification Kit (Qiagen) and, if necessary, used for further amplification. Low-abundant RNAs were amplified by nested PCR before gel-purification. Restriction sites for NotI were attached to PCR primers to allow subcloning of amplified cDNAs into the retroviral vectors pIE94-N/C-TAP thereby generating N- or C-terminal fusions with the TAP-tag (Rigaut et al., 1999, Nature Biotechnol. 17:1030-1032). N-terminal tagging was chosen for the following baits/entry points: Presenilin 2, Aph-1a, Pen-2, APP, Tau, Fe65. C-terminal tagging was chosen for the following baits/entry points: Nicastrin, Aph-1a, Aph-1b, APP695SW, APP-C99, Fe65, X11beta.

Clones were analyzed by restriction digest, DNA sequencing and by in vitro translation using the TNT T7 Quick Coupled Transcription/Translation System (Promega inc.). The presence of the proteins was proven by Western blotting using the protein A

part of the TAP-tag for detection. Briefly, separation of proteins by standard SDS-PAGE was followed by semi-dry transfer onto a nitrocellulose membrane (PROTRAN, Schleicher&Schuell) using the MultiphorII blotting apparatus from Pharmacia Biotech. The transfer buffer consisted of 48 mM Tris, 39 mM glycine, 10% methanol and 0,0375% sodium dodecylsulfate. After blocking in phosphate-buffered saline (PBS) supplemented with 10% dry milk powder and 0,1% Tween 20 transferred proteins were probed with the Peroxidase-Anti-Peroxidase Soluble Complex (Sigma) diluted in blocking solution. After intensive washing immunoreactive proteins were visualized by enhanced chemiluminescence (ECL; Amersham Pharmacia Biotech).

5.2 Preparation of Virus and infection

As a vector, a MoMLV-based recombinant virus was used.

The preparation has been carried out as follows:

5.2.1 Preparation of Virus

293 gp cells were grown to 100% confluency. They were split 1:5 on poly-L-Lysine plates (1:5 diluted poly-L-Lysine [0.01% stock solution, Sigma P-4832] in PBS, left on plates for at least 10 min.). On Day 2, 63 microgram of retroviral Vector DNA together with 13 microgram of DNA of plasmid encoding an appropriate envelope protein were transfected into 293 gp cells (Somia, et al., 1999, Proc. Natl. Acad. Sci. USA 96:12667-12672; Somia, et al. 2000, J. Virol. 74:4420-4424). On Day 3, the medium was replaced with 15 ml DMEM + 10% FBS per 15-cm dish. On Day 4, the medium containing viruses (supernatant) was harvested (at 24 h following medium change after transfection). When a second collection was planned, DMEM 10 % FBS was added to the plates and the plates were incubated for another 24 h. All collections were done as follows: The supernatant was filtered through 0.45 micrometer filter (Corning GmbH, cellulose acetate, 431155). The filter was placed into konical polyallomer centrifuge tubes (Beckman, 358126) that are placed in buckets of a SW 28 rotor (Beckman). The filtered supernatant was ultracentrifuged at 19400 rpm in the SW 28 rotor, for 2 hours at 21 degree Celsius. The supernatant was discarded. The pellet containing viruses was

resuspended in a small volume (for example 300 microliter) of Hank's Balanced Salt Solution [Gibco BRL, 14025-092], by pipetting up and down 100-times, using an aerosol-safe tip. The viruses were used for transfection as described below.

5,2.2 Infection

Cells that were infected were plated one day before into one well of a 6-well plate.

4 hours before infection, the old medium on the cells was replaced with fresh medium.

Only a minimal volume was added, so that the cells are completely covered (e.g. 700 microliter). During infection, the cells were actively dividing.

A description of the cells and their growth conditions is given in 5.2.3

To the concentrated virus, polybrene (Hexadimethrine Bromide; Sigma, H 9268) was added to achieve a final concentration of 8 microgram/ml (this is equivalent to 2.4 microliter of the 1 milligram/ml polybrene stock per 300 microliter of concentrated retrovirus). The virus was incubated in polybrene at room temperature for 1 hour. For infection, the virus/polybrene mixture was added to the cells and incubated at 37 degree Celsius at the appropriate CO₂ concentration for several hours (e.g. over-day or over-night). Following infection, the medium on the infected cells was replaced with fresh medium. The cells were passaged as usual after they became confluent. The cells contain the retrovirus integrated into their chromosomes and stably express the gene of interest.

5.2.3 Cell lines

The following Cell-lines were used:

Fe65-complex: HEK-293-cells, SKN-BE2-cells, SH-SY5Y-cells; X11beta-complex: HEK-293-cells, SKN-BE2-cells, SH-SY5Y-cells; Psen-2-complex: SKN-BE2-cells, SH-SY5Y-cells, LAN-cells; Nicastrin-complex: HEK-293-cells, SKN-BE2-cells; Aph-1a-complex: HEK-293-cells, SKN-BE2-cells; Pen-2-complex: HEK-293-cells, SKN-BE2-cells;

APP695SW-complex: HEK-293-cells, SKN-BE2-cells; APP-C99-complex: SKN-BE2-cells; Tau-complex: SKN-BE2-cells, SH-SY5Y-cells

SKN-BE2 cells (American Type Culture Collection-No. CRL-2271) were grown in 95% OptiMEM + 5% iron-supplemented calf serum.

SH-SY5Y-cells were grown in 85% DMEM/F-12, 15% FBS, Non-essential AA LAN-cells (human neuroblastoma cell line) were grown in 90% RPMI 1640 + 10% FBS

The expression pattern of the TAP-tagged proteins was checked by immunoblotanalysis as described in 5.3.3 and/or by immunofluorescence as described in 5.3.1 or 5.3.2.

5.3 Checking of expression pattern of TAP-tagged proteins

The expression pattern of the TAP-tagged protein was checked by immunoblot analysis and/or by immunofluorescence. Immunofluorescence analysis was either carried out according to section 5.3.1 or to section 5.3.2 depending on the type of the TAP-tagged protein. Immunoblot analysis was carried out according to section 5.3.3.

5.3.1 <u>Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for plasma membrane and ER bound proteins</u>

Cells were grown in FCS media on polylysine coated 8 well chamber slides to 50% confluency. Then fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4). The cells were incubated for 30 minutes at room temperature in 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at room temperature. Blocking was performed with 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at room temperature. Incubation of the primary antibodies was performed in the blocking solution overnight at +4°C. The proper dilution of the antibodies was determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin for 2x 20 minutes at room temperature. Incubation of the

secondary antibodies is performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes). Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin was used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were then washed again 2x 20 minutes at room temperature in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

5.3.2 <u>Protocol for the indirect Immunofluorescence staining of fixed mammalian cells for non-plasma membrane bound proteins:</u>

Cells were grown in FCS media on Polylysine coated 8 well chamber slides to 50% confluency. Fixation of the cells was performed in 4% ParaFormAldehyde diluted in Phosphate Buffer Saline (PBS) solution (0.14M Phosphate, 0.1M NaCl pH 7.4) for 30 minutes at Room Temperature (RT), 300 microliters per well. Quenching was performed in 0.1M Glycine in PBS for 2x 20 minutes at roon temperature. Permeabilization of cells was done with 0.5% Triton X-100 in PBS for 10 minutes at room temperature. Blocking was then done in 1% Bovine Serum Albumin (BSA) in 0.3% Saponin + PBS for at least 1 hour at RT (Blocking solution). Incubation of the primary antibodies was performed in the blocking solution, overnight at +4°C. The proper dilution of the antibodies has to be determined in a case to case basis. Cells were washed in PBS containing 0.3% Saponin, for 2x 20 minutes at RT. Incubation of the secondary antibodies was performed in the blocking solution. Alexa 594 coupled goat anti-rabbit is diluted 1:1000 (Molecular Probes), Alexa 488 coupled goat anti-mouse is diluted 1:1000 (Molecular Probes). DAPI was used to label DNA. If Phalloidin is used to label F-actin, the drug is diluted 1:500 and incubated with the secondary antibodies. Cells were washed 2x 20 minutes at RT in PBS. The excess of buffer was removed and cells were mounted in a media containing an anti-bleaching agent (Vectashield, Vector Laboratories).

5.3.3 Immunoblot analysis

To analyze expression levels of TAP-tagged proteins, a cell pellet (from a 6-well dish) was lyzed in 60-µl-DNAse I buffer (5% Glycerol, 100 mM NaCl, 0.8 % NP-40 (IGEPAL), 5 mM magnesium sulfate, 100 μ g/ml DNAse I (Roche Diagnostics), 50 mM Tris, pH 7.5, protease inhibitor cocktail) for 15 min on ice. Each sample was split into two aliquots. The first half was centrifuged at 13,000 rpm for 5 min. to yield the NP-40extractable material in the supernatant; the second half (total material) was carefully triturated. 50 μg each of the NP-40-extractable material and the total material are mixed with DTT-containing sample buffer for 30 min at 50°C on a shaker and separated by SDS polyacrylamide gel electrophoresis on a precast 4-12% Bis-Tris gel (Invitrogen). Proteins were then transferred to nitrocellulose using a semi-dry procedure with a discontinuous buffer system. Briefly, gel and nitrocellulose membrane were stacked between filter papers soaked in either anode buffer (three layers buffer A1 (0.3 M Tris-HCI) and three layers buffer A2 (0.03 M Tris-HCI)) or cathode buffer (three layers of 0.03 M Tris-HCI, pH 9.4, 0.1 % SDS, 40 mM ε-aminocapronic acid). Electrotransfer of two gels at once was performed at 600 mA for 25 min. Transferred proteins were visualized with Ponceau S solution for one min to control transfer efficiency and then destained in water. The membrane was blocked in 5% non-fat milk powder in TBST (TBS containing 0.05% Tween-20) for 30 min at room temperature. It was subsequently incubated with HRPcoupled PAP antibody (1:5000 diluted in 5% milk/TBST) for 1 h at room temperature, washed three times for 10 min in TBST. The blot membrane was finally soaked in chemiluminescent substrate (ECL, Roche Diagnostics) for 2 min. and either exposed to X-ray film or analyzed on an imaging station.

5.4 Purification or protein complexes

Protein complex purification was adapted to the sub-cellular localization of the TAP-tagged protein and was performed as described below.

5.4.1 Lysate preparation for cytoplasmic proteins

About 1 x 10⁹ adherent cells (average) were harvested with a cell scrapper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid

nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of CZ lysis buffer (50 mM Tris-Cl, pH 7.4; 5 % Glycerol; 0,2 % IGEPAL; 1.5 mM MgCl₂; 100 mM NaCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was incubated for 30 min on ice and spun for 10 min at 20,000g. The supernatant was subjected to an additional ultracentrifugation step for 1 h at 100,000g. The supernatant was recovered and rapidly frozen in liquid nitrogen or immediately processed further.

5.4.2 Lysate preparation for membrane proteins

About 1 x 10⁹ adherent cells (average) were harvested with a cell scrapper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Membrane-Lysis buffer (50 mM Tris, pH 7.4; 7.5 % Glycerol; 1 mM EDTA; 150 mM NaCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (CompleteTM, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 750g, the supernatant was recovered and subjected to an ultracentrifugation step for 1 h at 100,000g. The membrane pellet was resuspended in 7,5 ml of Membrane-Lysis buffer containing 0.8% n-Dodecyl-β-D-maltoside and incubated for 1 h at 4°C with constant agitation. The sample was subjected to another ultracentifugation step for 1h at 100,000g and the solubilized material was quickly frozen in liquid nitrogen or immediately processed further.

5.4.3 Lysate preparation for nuclear proteins

About 1 x 10⁹ adherent cells (average) were harvested with a cell scrapper and washed 3 times in ice-cold PBS (3 min, 550g). Collected cells were frozen in liquid nitrogen or immediately processed further. For cell lysis, the cell pellet was resuspended in 10 ml of Hypotonic-Lysis buffer (10 mM Tris, pH 7.4; 1.5 mM MgCl₂; 10 mM KCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor

cocktail (Complete™, Roche) per 25 ml of buffer) and homogenized by 10 strokes of a tight-fitted pestle in a dounce homogenizer. The lysate was spun for 10 min at 2,000g and the resulting supernatant (S1) saved on ice. The nuclear pellet (P1) was resuspended in 5 ml Nuclear-Lysis buffer (50 mM Tris, pH 7.4; 1.5 mM MgCl₂; 20 % Glycerol; 420 mM NaCl; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT; containing 1 tablet of EDTA-free Protease inhibitor cocktail (Complete™, Roche) per 25 ml of buffer) and incubated for 30 min on ice. The sample was combined with S1, further diluted with 7 ml of Dilution buffer (110 mM Tris, pH 7.4; 0.7 % NP40; 1.5 mM MgCl₂; 25 mM NaF; 1 mM Na₃VO₄; 1 mM DTT), incubated on ice for 10 min and centrifuged at 100,000g for 1h. The final supernatant (S2) was frozen quickly in liquid nitrogen.

5.4.4 Tandem Affinity Purification

The frozen lysate was quickly thawed in a 37°C water bath, and spun for 20 min at 100,000g. The supernatant was recovered and incubated with 0.2 ml of settled rabbit lgG-Agarose beads (Sigma) for 2 h with constant agitation at 4°C. Immobilized protein complexes were washed with 10 ml of CZ lysis buffer (containing 1 Complete™ tablet (Roche) per 50 ml of buffer) and further washed with 5 ml of TEV cleavage buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0.1 % IGEPAL; 0.5 mM EDTA; 1 mM DTT). Proteincomplexes were eluted by incubation with 5μ l of TEV protease (GibcoBRL, Cat.No. 10127-017) for 1 h at 16°C in 150 μ l TEV cleavage buffer. The eluate was recovered and combined with 0.2 ml settled Calmodulin affinity beads (Stratagene) in 0.2 ml CBP binding buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0,1 % IGEPAL; 2mM MgAc; 2mM Imidazole; 1mM DTT; 4 mM CaCl₂) followed by 1 h incubation at 4°C with constant agitation. Immobilized protein complexes were washed with 10 ml of CBP wash buffer (10 mM Tris, pH 7.4; 100 mM NaCl; 0,1 % IGEPAL; 1mM MgAc; 1mM Imidazole; 1mM DTT; 2 mM CaCl₂) and eluted by addition of 600 μ l CBP elution buffer (10 mM Tris, pH 8.0; 5 mM EGTA) for 5 min at 37°C. The eluate was recovered in a siliconzed tube and lyophilized. The remaining Calmodulin resin was boiled for 5 min in 50 μ l 4x Laemmli sample buffer. The sample buffer was isolated, combined with the lyophilised fraction and loaded on a NuPAGE gradient gel (Invitrogen, 4-12%, 1.5 mm, 10 well).

5.4.5 Isolation of the Sambiasin complex of the invention from mouse tissue

Two mouse forebrains (0.6314 g total wet weight) were lysed in 14 mls of 50 mM HEPES pH 7.4; 150 mM NaCl; 1 mM EDTA; 0.5 mM Sodium Vanadate; 10% Glycerol; 1% n-Dodecyl-β-D-maltoside containing standard proteinase inhibitors. The tissue was homogenised in a Warring blender for 30 seconds on ice. Homogenates were incubated on ice for 1 hour and then centrifuged at 13,000 g for 30 min at 4°C. The resulting pellet was stored at -80°C while the supernatant was centrifuged at 50,000 g for 30 min at 4°C and the resulting pellet was also stored at -80°C. 6.5 ml of the supernatant from this second centrifugation step was taken and combined with 25 μ l of anti presenilin-1 antisera (MAB5232, Chemicon). The antibody/lysate mixture was incubated for 1 hour at 4°C with end-over end mixing. Pre-washed protein G sepharose was added and the mixture was incubated overnight at 4°C with end-over mixing. The protein G was recovered by centrifugation at 200 g for 5 min at 4°C. The protein G beads were then washed 5 times in 1ml lysis buffer (containing 0.1% n-Dodecyl-β-D-maltoside rather than 1%). 100 μ l of NuPAGE sample buffer (Invitrogen) was added and the sample incubated at 37°C for 10 min. Samples were separated on 4-12 % NuPAGE bis/tris gels (Invitrogen, 1.5 mm, 10 well). Proteins were visualized by staining with colloidal coomassie (Sigma) and then analysed by LC/MSMS.

5.5 Protein identification by mass spectrometry

5.5.1 Protein digestion prior to mass spectrometric analysis

Gel-separated proteins were reduced, alkylated and digested in gel essentially following the procedure described by Shevchenko et al., 1996, Anal. Chem. 68:850-858. Briefly, gel-separated proteins were excised from the gel using a clean scalpel, reduced using 10 mM DTT (in 5mM ammonium bicarbonate, 54°C, 45 min) and subsequently alkylated with 55 mM iodoacetamid (in 5 mM ammonium bicarbonate) at room temperature in the dark (30 min). Reduced and alkylated proteins were digested in gel with porcine trypsin (Promega) at a protease concentration of 12.5 ng/ μ l in 5mM ammonium bicarbonate. Digestion was allowed to proceed for 4 hours at 37°C and the reaction was subsequently stopped using 5 μ l 5% formic acid.

5.5.2 Sample preparation prior to analysis by mass spectrometry

Gel plugs were extracted twice with 20 μ l 1% TFA and pooled with acidified digest supernatants. Samples were dried in a a vaccum centrifuge and resuspended in 13 μ l 1% TFA.

5.5.3 Mass spectrometric data acquisition

Peptide samples were injected into a nano LC system (CapLC, Waters or Ultimate, Dionex) which was directly coupled either to a quadrupole TOF (QTOF2, QTOF Ultima, QTOF Micro, Micromass or QSTAR Pulsar, Sciex) or ion trap (LCQ Deca XP) mass spectrometer. Peptides were separated on the LC system using a gradient of aqueous and organic solvents (see below). Solvent A was 5% acetonitrile in 0.5% formic acid and solvent B was 70% acetonitrile in 0.5% formic acid.

Time (min)		
	% solvent A	% solvent B
0	95	5
5.33	92	8
35	50	50
36	20	80
40	20	80
41	95	5
50	95	5

Peptides eluting off the LC system were partially sequenced within the mass spectrometer.

5.5.4 Protein identification

The peptide mass and fragmentation data generated in the LC-MS/MS experiments were used to query fasta formatted protein and nucleotide sequence databases maintained and updated regularly at the NCBI (for the NCBInr, dbEST and the

human and mouse genomes) and European Bioinformatics Institute (EBI, for the human, mouse, D. melanogaster and C. elegans proteome databases). Proteins were identified by correlating the measured peptide mass and fragmentation data with the same data computed from the entries in the database using the software tool Mascot (Matrix Science; Perkins et al., 1999, Electrophoresis 20:3551-3567). Search criteria varied depending on which mass spectrometer was used for the analysis.

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

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TABLE 1

COMPONENTS OF COMPLEXES

1743

unknown function APP-C99 Proteins of sub-family B, member ATP-binding cassette, 14-3-3 protein gamma 14-3-3 protein epsilon Known internactors of the Novel interactors of 14-3-3 protein eta 14-3-3 protein tau 14-3-3 protein 14-3-3 protein the complex zeta/delta APP-C99 beta/alpha APP-C99 complex APLP2 APLP1 APP sub-family B, member 7 14-3-3 protein beta/alpha 14-3-3 protein zeta/delta 14-3-3 protein gamma ATP-binding cassette, 14-3-3 protein epsilon All interactors of the 14-3-3 protein eta 14-3-3 protein tau APP-C99 APLP2 complex APLP1 APP Point **Entry** Fe65 Name of complex complex Fe65-

							IP100104084.1	Krab box protein	ensp00000302970							Protein similar to	probable mitotic	centromere	associated kinesin			
ECP-51		GAP-associated	tyrosine	phosphoprotein p62	Integral membrane	protein 2B (ITM2B)	IP100104084.1	Krab box protein	ensp00000302970	PDZ domain protein	MAGI-3	70000	PPPZHBA (PP2A, 55	kDa regulatory subunit	B, alpha)	Protein similar to		centromere associated			SAP-62	
	Fe65																			RNB6		Transcription factor CP2
ECP-51	Fe65	GAP-associated tyrosine	phosphoprotein p62		Integral membrane	protein 2B (ITM2B)	IP100104084.1	Krab box protein	ensp00000302970	PDZ domain protein	MAGI-3	PPP2RBA (PP2A, 55		KDa regulatory subunit B,	alpha)	Protein similar to	probable mitotic	centromere associated	kinesin	RNB6	SAP-62	Transcription factor CP2 T

nc finger protein	ADAMTS-19				BAT1	Coonf11 (sim to a		region of MANBPINI)	Cadherin EGF LAG	seven-pass G-type	receptor 2		0	Caisyntenin-z	Calsyntenin-3	CGB0_HUMAN						
Zinc finger protein 277 Zinc finger protein 277	ADAMTS-19 AI	APLP1	•	Axonemal dynein					Cadherin EGF LAG C			Caleymtanin-1		Calsyntenin-2	Calsyntenin-3	CGB0_HUMAN	Chandraitin culfate		proteoglycan o	Chromatin-specific	transcription elongation	
Z			АРР																ļ			
Zinc finger protein 277	ADAMTS-19	APLP1	APP	Axonemal dynein heavy	chain 8	BAT1	C20orf11 (sim to a	region of RANBPM)		Cadherin EGF LAG	seven-pass G-type	receptor 2	Calsyntenin-1	Caleymtenin-2	Calpintonin-3	Calsymening	CGBO_HUMAIN	Chondroitin sulfate	proteoglycan 6	Chromotin-enocific	Ciliotiating elongation	וומווארוויייון כוכוואריייי
	X11b																		_			
	X11b-	complex									·											

			Dkfzp586c1924				ENG00000168820	(hypothetical protein	with p-loop)					FLJ13910							HERC2 protein
factor FACT 140 kDa	subunit	DC6 protein	Dkfzp586c1924	Dynein light chain 2A	Dynein light chain-A	ELAVL3	ENG00000168820	(hypothetical protein	with p-loop)	Eukaryotic translation	initiation factor 4A,	isoform	Filamin, gamma	FLJ13910	FRAP1	GTP-binding protein	ERA	HADH2/ERAB	(mitochondrial enzyme)	HDAC2	HERC2 protein
											-										
factor FACT 140 kDa	subunit	DC6 protein	Dkfzp586c1924	Dynein light chain 2A	Dynein light chain-A	ELAVL3	ENG00000168820	(hypothetical protein with	(dool-d	Eukaryotic translation	initiation factor 4A,	isoform	Filamin, gamma	FLJ13910	FRAP1	GTP-binding protein	ERA	HADH2/ERAB	(mitochondrial enzyme)	HDAC2	HERC2 protein

Neurexin-1

		TYK2		TYK2	•
		Ubiquitin-protein ligase		Ubiquitin-protein ligase	Ubiquitin-protein
		E3-alpha		E3-alpha	ligase E3-alpha
		VGF nerve growth factor		VGF nerve growth	
	-	inducible protein		factor inducible protein	
		X11beta	X11beta		
		Zinc finger protein 198		Zinc finger protein 198	
PSEN2-	PSEN2	18 kDa microsomal		18 kDa microsomal	
complex		signal peptidase subunit		signal peptidase	
				subunit	
		200 kDa proteasome		200 kDa proteasome	
		activator		activator	
		ABCB11		ABCB11	
		Acetolactate synthase		Acetolactate synthase	
		homolog		homolog	
		Adrenoleukodystrophy		Adrenoleukodystrophy	
		protein		protein	
		Aph-1a	Aph-1a		
		ATM		ATM	
		ATP7A		ATP7A	
		ATP-binding cassette		ATP-binding cassette	
		protein, sub-family B,		protein, sub-family B,	

	member 1	member 1	
	to open and the state of the st	ATP-dependent	
	ATP-dependent	Hata ascatoroclictor	
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+	BIG1	BIG1	·
-	BTAF1	BTAF1	
	Calcium-hinding protein	Calcium-binding	
	Dog	protein P22	
	Cation-chloride	Cation-chloride	
	ootranenorder-interacting	cotransporter	
	profein	interacting protein	
		CD97	
	CDB/	NAMILL	COM HUMAN
	CDM_HUMAN	NIAMOH_IMOO	
	Centromere/kinetochore	Centromere/kinetochor	
	protein ZW10 homolog	e protein ZW10	
		bomolog	
+	Cerebral protein 10	Cerebral protein 10	Cerebral protein 10
	CGI-13	CGI-13	CGI-13
	2 3	CGI-51	CGI-51
	CGI-51		
	cholinergic receptor,	cholinergic receptor,	
	nicotinic, alpha	nicotinic, alpha	
	polypeptide 3	polypeptide 3	

			OKEZEE0624004	DN-2p30001924				ensnOOOOOO	(hynothetical protein	with n-loop	dond		FLJ20342	FLJ20420	FLJ22555	FLJ22678							
CHRNA3	DAAM1	DAPK1	DKFZn586c1924		Down syndrome critical	region protein 2	ECSIT	ensp00000297280	(hypothetical protein	with p-loop)	FACL 1	E1 100040	FLJZU342	FLJ20420	FLJ22555	FLJ22678	Galactosylgalactosylxyl	osylprotein 3-beta-	glucuronosvitransferas	80 O	HTRA2	HI-K4	
				роскз																			
CHRNA3	DAAM1	DAPK1	DKFZp586c1924	роскз	Down syndrome critical	region protein 2	ECSIT	ensp00000297280	(hypothetical protein with	(dool-d	FACL1	FLJ20342	E 190490	רבשבטיים	rLJ22555	FLJ22678	Galactosylgalactosylxylo	sylprotein 3-beta-	glucuronosyltransferase	က	HTRA2	HU-K4	

		XH]	Hypothetical protein	Hypothetical protein
	Hypothetical protein	Ī		FI,123356
	FLJ23356	1	寸	
	Uwothetical profein	IAH	Hypothetical protein	Hypothetical protein
	Hypoti jeticai process	KI		KIAA0455
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	KIAA0971-I	N N		KIAA0971-1
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	HYPOINETIONE	<u>ц</u>	4405.	PROTEIN
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	KIAA0103		2707070	MGC4248
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	MGC5442	×	MGC5442	MGC3446
	Nicastrin	Nicastrin		
	NICE-3	Z	NICE-3	NICE-3
	NPC1	2	NPC1	
	NPDOOP	Z	NPD002	
	to topograme A 1714	2	NPL4, a component of	NPL4, a component
	NPL4, a component of		the nuclear pore	of the nuclear pore
	the nuclear pore complex		complex	complex

P63 protein		Prohibitin	PSMA1	PSMA3	PSMA4	PSMA6	PSMB1	PSMB2	PSMB3	PSMB4	PSMB5	PSMB6	OGINO 1	PSMC1	PSMC2	PSMC3	PSMC4	PSMC5	PSMC6	PSMD1	PSMD11	PSMD12	!
	Presenllin 2																						
P63 protein	Presenilin 2	Prohibitin	PSMA1	PSMA3	PSMA4	PSMA6	PSMB1	PSMB2	PSMB3	PSMB4	PSMB5	PSMB6	PSMC1	DOMOG	T SIMICE	PSMC3	PSMC4	PSMC5	PSIMC6	PSMD1	PSMD11	PSMD12	

			PSMD13	PSMD13	
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STRA6 isoform 1 Tparl Ubiquitin-protein ligase EDD EDD Channel 2 Wolframin Nicastrin 18 kDa microsomal			Stearoyl-CoA desaturase	Stearoyl-CoA	
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EDD Voltage-dependent anion channel 2 Wolframin Nicastrin 18 kDa microsomal			Ubiquitin-protein ligase	Ubiquitin-protein lig	es
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Nicastrin 18 kDa microsomal			Wolframin	Wolframin	
		Nicastrin	18 kDa microsomal	18 kDa microsom	

complex	signal peptidase subunit		signal peptidase	
		,	subunit	1,1
	25 kDa microsomal		25 kDa microsomal	
	signal peptidase subunit		signal peptidase	
			subunit	
	Aph-1a	Aph-1a		
	ATP-binding cassette,		ATP-binding cassette,	ATP-binding
	sub-family A, member 3		sub-family A, member	cassette, sub-family
			က	A, member 3
	BACE1	BACE1		-
	BSCv protein		BSCv protein	
	(FRAGMENT)		(FRAGMENT)	
	CAMK4		CAMK4	
	Casein kinase II beta		Casein kinase II beta	
	chain		chain	
	Cathepsin B		Cathepsin B	
	CGI-13		CGI-13	CGI-13
	DCTN1		DCTN1	
	Delta-6 fatty acid		Delta-6 fatty acid	
	desaturase		desaturase	
	ENSG00000144840		ENSG00000144840	ENSG00000144840
	FACL3		FACL3	

EACI 4			FLJ20342 FLJ20342	FLJ20481 FLJ20481	FLJ22390 FLJ22390	homolog of yeast golgi	membrane protein		yif1p (yip1p-interacting	factor)	ICAM-2	KIAA0095 KIAA0095	KIAA0922		KIAA1181 KIAA1181	(FRAGMENT) (FRAGMENT)	KIAA1533 KIAA1533	(FRAGMENT) (FRAGMENT)	Mesenchymal stem cell	protein DSCD75		Neurotrypsin		NICE-3	PAS domain containing	
	FACL4	FLJ13977	FI.120342	EI 120481	E1 122390			membrane protein yif1p	(yip1p-interacting factor)		ICAM-2	121 A 2000 A 121	KIAAUUSS	KIAA0922	KIAA1181 (ERAGMENT)	-	WAAAFOO (FDACMENIT)	NIAA 1959 (Tradination)	القم سمئه امسامات		protein Docura	Neurotrypsin	Nicastrin	NICE-3	Edition of the second	PAS domain containing

serine/threonine kinase	serine/threonine kinase	es
	Pen-2	
PP1, regulatory subunit	PP1. regulatory sur	PP1. regulatory Surbunit PP1 regulatory
	158	Subunit 15B
Presenilin-1	Presenilin-1	
Presenilin-2	Presenilin-2	
Protein amplified in	Protein amplified in	
osteosarcoma (OS-9)	osteosarcoma (OS-9)	
Protein similar to stromal	Protein similar to	
cell-derived factor 2	stromal cell-derived	
	factor 2	
Protocadherin beta 8	Protocadherin beta 8	
REP8 protein	REP8 protein	
Retinal short-chain	Retinal short-chain	
dehydrogenase/reductas	dehydrogenase/reduct	-
e retSDR2	ase retSDR2	
RING finger protein 5	RING finger protein 5	RING finger protein 5
Stromal cell-derived	Stromal cell-derived	
factor 2-like 1	factor 2-like 1	
Thioredoxin domain-	Thioredoxin domain-	Thioredoxin domain-
containing protein	containing protein	containing protein
tyrosine phosphatase	tyrosine phosphatase	tyrosine phosphatase

ensg00000149185									ABCC1	Acataloniato	Acelolacials	synthase homolog								ATD hinding		cassette, suo-rarmy	A member 3		
ensg00000149185	18 kDa microsomal	signal peptidase	subunit	23 kDa microsomal	signal peptidase	25 kDa microsomal	signal peptidase	subunit	ABCC1		Acetolactate synthase	homolog	API P2			АРР	ATM	ATP1B1	ATP2C1		ATP-binding cassette,	sub-family A member 3 cassette, sub-rarmy	·	Brain-specific GTP-	
															Aph-1a										
Approprietation 149185	18 kDa microsomal	ionol nontidasa subunit	signal pepulase sasami	23 kDa microsomal	signal peptidase	25 kDa microsomal	signal nentidase subunit			ABCC1	Acetolactate synthase	homolog	Boologia	APLP2	Aph-1a	АРР	ATM	ATP1R1		ATP2C1	ATP-binding cassette,	enh-family A member 3			Brain-specific GTP-
		Apn-1a					•											-							
		Aph-1a-	complex										-			·									

orotein	CDW92	protein-10			olate	Q.		Endocytic receptor					0	GPR49								uie	TICAL al protein	TICAL	TICAL	TICAL
hinding protein	CDW92	Cerebra	CGI-13	CNTNAP1	Dihydrofolate	reductase	DNM1	Endocyt	Endo180	ENG	EXT2	ЕХТСЗ	FLJ13660	GPR49	HK2	HU-K4	HUNC18a	_	HYPOTH	HYPOTHETICAL PROTEIN	HYPOTH PROTEIN Hypotheti	HYPOTH PROTEIN Hypotheti	HYPOTH PROTEIN Hypotheti	HYPOTH PROTEIN Hypotheti	HYPOTH PROTEIN Hypotheti	HYPOTHE PROTEIN Hypothetica (Fragment)
binding protein	CDW92	Cerebral protein-10	CGI-13	CNTNAP1	Dihydrofolate reductase		DNM1	Endocytic receptor	Endo180	ENG	EXT2	ЕХТГЗ	FLJ13660	GPR49	HK2	HU-K4	HUNC18a		HYPOTHETICAL	HYPOTHETICAL PROTEIN		⊢ ∣≂	⊢ ∣≂	⊢ ∣≂	⊢	⊢

		Hypothetical protein H	Hypothetical protein
	Hypothetical protein		FLJ14562
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	MGC10924 Similar to		Nedd4 WW-binding
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	integral membrane	integral memorane	
	transporter protein	transporter protein	transporter protein
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	ITPR1		

(FRAGMENT) KIAA0251 (FRAGMENT) KIAA0363 (FRAGMENT) KIAA0363 (FRAGMENT) KIAA0363 KIAA0363 KIAA0763 Mesenchymal stem cell protein DSCD75 MGC4248 PCDHA10 PCDHB12 PCDHB13:	(FRAGMENT) (FRAGMENT) KIAA0251 KIAA0251 KIAA0251 KIAA0251 KIAA0251 KIAA0251 KIAA0251 KIAA0251 KIAA0363 KIAA0363 KIAA0363 KIAA0363 KIAA0363 KIAA0371 KIAA0971 KIAA010 FODHA10 PCDHA10 PCDHB12 PCDHB13: PCDHB13: PCDHB13: PCDHB13:	Nicastrin	KIAA0251 (FRAGMENT) KIAA0363 (FRAGMENT) KIAA0763 KIAA0763 KIAA0971 KIAA1250 LRP5 Mesenchymal stem cell protein DSCD75 MGC4248 Neurotrypsin Nicastrin Nicastrin NPP2 PCDHA10 PCDHB12 PCDHB13:
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PCDHB12			PCDHB12
PCDHA10	PCDHA10		
	חרחח		PCDHA10
	NRP2		NRP2
		vicasuli	
		licoptuin	
	Neurotrypsin		Neurotrypsin
MGC4248	MGC4248		MGC4248
cell protein DSCD7	protein DSCD75		protein DSCD/5
Mesenchymal sterr	wesencnymai stem cell		
			Mesenchymal etem cell
	LRP5		LRP5
KIAA1250	KIAA1250		KIAA1250
KIAA0971	KIAA0971		KIAA0971
KIAA0763	KIAA0763		NIAAU703
(FRAGMENT)	(THAGIMENT)		071A A 0720
KIAA0363	KIAA0363		
(FRAGMENT)	(FRAGMENT)		
KIAA0251	KIAA0251		
(FRAGMENT)	(FRAGMENT)		- 1.
NIAAUUDZ	NAAUU02		

			Similar to CGL-135	nrotein			Sterile alpha and	HEAT/Armadillo motif	protein					tegt: testis enhanced	gene transcript (bax	inhibitor 1)	Thioredoxin domain-	containing protein				
	activator of	transcription-1	Similar to CGI-135	protein	SMAP-1B	SPTLC2	Sterile alpha and	HEAT/Armadillo motif	protein	Sterol O-	acyltransferase 1	STMN3	todic cited that	regi. testis ennanced	gene transcript (bax	inhibitor 1)	Thioredoxin domain-	containing protein	Triple functional	domain nrotein	(PTPRF interacting)	UNCSC
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Software of transfer	activator of transcription-	-	Similar to CGI-135	protein	SMAP-1B	SPTLC2	Sterile alpha and	HEAT/Armadillo motif	protein	Sterol O-acyltransferase	-	STMN3	tegt: testis enhanced		gene transcript (bax	inhibitor 1)	Thioredoxin domain-	containing protein	Triple functional domain	protein (PTPRF	interacting)	UNCSC
					·												-					

brane	sector associated	protein m8-9			V391 HUMAN				COPINE FAMILY	MEMBER.					KIAA1102		(Fragment)	MGC2803						
thase	membrane sector associated protein m8- sector		vacuolar protein sorting	protein 18	NAI		Alpha-2 catenin		CODINE FAMILY COL			Copine III	Dachshund 2	Delta-1 catenin	mont	אואן (אופווופּמיזי) צטרראאןאן בי	(F)	MGC2803 MG					Presenilin 2	
>	<u>E 0</u>	6	<u>></u>	9				 Anh.1a												Nicastrin	Pen-2	Presentlin 1		
Vacuolar ATP synthase	membrane sector	associated protein mo-9	Scillage State of the State of	vacuolar protein sorung	protein 18	Y391_HUMAN	Alpha-2 catenin			COPINE FAMILY	MEMBER.	Cooine III	O political O	Dagrishiung	Delta-1 catenin	KIAA1102 (Fragment)			MGCZ803	Nicastrin	Pen-2	Presenilin 1		Preseniin 2
							Pen-2- Pen-2	 contined	***************************************															

TNBC15							FLJ10773																
TNRC15	TPST1	ZIP kinase					FLJ10773		IL13RA2	Integral membrane	protein 2B (ITM2B)	(C.S.)	Integral membrane	transporter protein		S-100 alpha		VDD			CAMKOD		Delta-like homolog
		-	APP695SW		Fe65	Fe65L1									JIP-1		X11beta			APP-C99			
TNRC15	TPST1	ZIP kinase	APP695SW		Fe65	Fe65L1	FLJ10773	GTF2I	IL13RA2	Integral membrane	protein 2B (ITM2B)	Integral membrane	יייילפים יייפווטומום	transporter protein	JIP-1	S-100 alpha	X11beta	АРР		APP-C99	CAMK2D	Delta-like homolog	R
			APP695S	>														APP-C99					
			APP695SW-	complex														APP-C99-	complex				7

				KIAA1102		(Fragment)	KIAA1949	MGC4022	MGC5442																				
		Integral membrane	transporter protein	VIA A 4 4 00 (Eracmont)	KIAAT 102 (Flayinein)		KIAA1949	MGC4022	- Totalia	MGC544Z	NAP-1 related protein	Meurocalcin delta		REST corepressor	S-100 alpha		S-100 beta								Deoxyhypusine		synthase	Dynactin 2	
Fe65	Fe65L1																		X11beta	14-3-3 protein zeta/delta	witz A	Actin	Alpha tubulin	Beta tubulin					
Fe65	-		integral membrane	transporter protein	KIAA1102 (Fragment)			KIAA1949	MGC4022	MGC5449		NAP-1 related protein	Neurocalcin delta	TOPSOTOSOC TOTAL	HEST COTEDIESSOL	S-100 alpha	0 400 boto	S-100 pera	X11beta	otein zeta/delta		Actin	Alpha tubulin	Dota tubilin	חפום ומסמייי	Deoxyhypusine synthase			Dynactin 2
																				}-	Tau-complex I au		+						

	MEP50		MEDEN	Marion
			ואובו פס	OCTUR
-	Nuclear receptor co-		Nuclear receptor co-	•
	repressor/HDAC3		repressor/HDAC3	
	complex subunit TBLR1		complex subunit	
			TBLR1	
	PPP2CA (PP2A,	PPP2CA (PP2A, catalytic		
	catalytic subunit, alpha)	subunit, alpha)		
	PPP2CB (PP2A,	PPP2CB (PP2A, catalytic		
	catalytic subunit, beta)	subunit, beta)		
	PPP2R1A (PP2A, 65	PPP2R1A (PP2A, 65 KDA		
	KDA regulatory subunit	regulatory subunit A, alpha)		
	A, alpha)			
	PPP2RBA, (PP2A, 55	PPP2RBA, (PP2A, 55 KDA		
	KDA regulatory subunit	regulatory subunit B, alpha)		
	B, alpha)			
	S-100 beta		S-100 beta	
	Tau	Tau		

INDIVIDUAL PROTEINS OF THE COMPLEXES

	SEQ ID	IPI number	Molecular weight
Protein name		19100000016.1	29174
14-3-3 protein epsilon	_		00000
11.00 attacks and alpha	8	IPI00216318.1	28082
14-3-3 protein beta/aipria	8	IPI00216319.1	28219
14-3-3 protein eta	4	IP100220642.1	28303
14-3-3 protein gamma	5	IP100018146.1	27764
14-3-3 protein tau	9	IP100021263.1	27745
14-3-3 protein zeta/delta	, ,	1500104108 1	20625
18 kDa microsomal signal peptidase subunit	3	1100104120.1	2000
oco Po protessome activator	101	IP100005260.1	206407
SOU NDA PIOCESSON CONTRACTOR CONT	221	IP100030262.2	20253
23 kDa microsomai signai pepilidase	10,	10100014148 1	25003
25 kDa microsomal signal peptidase subunit	22	1100014140.1	
	102	IP100030011.1	146393
ABCBII	222	IP100008338.1	164941
ABCC1	107	101000000000000000000000000000000000000	67868
Acetolactate synthase homolog	201	11-100000001-11	20277
A city	302	IP100021439.1	41 /3/
Acur	25	IP100152639.1	134062
ADAMTS-19	95	10100017637 1	82909
Adrenoleukodystrophy protein	9	10001	70450
Alpha tribulio	306	IP100142632.1	20100
אונות ומסמוויו			

.

TABLE 2

Alpha 9 actualia			
Aprilar Catellin	280	IP100030907.1	105282
Aph-1a	109	IPIOOSOGEA 1	28006
APLP1	,	1.100000001.1	70330
API D2	,	IPI00020012.1	72176
ADD	&	IP100031030.1	86956
ADBEGEORY	6	IP100006608.1	86943
WINDSDAM	290	CZB00000007.1	78630
APP-C99	9	CZB00000004.1	11277.9
АТМ	5		
ATP181	201	IP100012732.1	350644
ATPOCI	223	IP100006484.1	35061
ATB7A	224	IP100024344.1	100576
	106	IP100028610.1	163335
ATP-binding cassette protein, sub-family B, member 1	104		141463
ATP-binding cassette, sub-family A member 3	186		191388
ATP-binding cassette, sub-family B, member 7	11		R9641
ATP-dependent metalloprotease FtsH1 homolog	202		1
Axonemal dynain booms obein a	3	Ir100045846.1	86503
PACE-	26	IP100014845.4	516063
BAT1	187	IPI00011518.1	55764
Bata tubulin	27	IP100218291.1	53243
	307	IP100142634.1	49671

		I		
	110	IP100002188.1	208709	
Big1	225	IP100103530.1	63543	
Brain-specific G I P-binding protein	188	IP100031131.1	46480	
BSCv protein (FRAGMENT)	111	IP100024802.1	206887	
BTAF1 C20nd11 (sim to a region of RANBPM)	28	IP100016634.1	26749	
Cadherin EGF LAG seven-pass G-type receptor 2	30	IP100015346.1	317453	
	117	IPI00218924.1	22456	,
Calcium-binding protein r22	31	IP100007257.1	109793	
Calsyntenin-1	32	IP100005491.1	107020	
Calsyntenin-2	33	IP100156997.1	106098	
Calsyntenin-3	297	IP100013787.1	56297	57
CAMK2D	189	IP100002921.1	51926	/5 T
CAMK4	9	IP100010865.1	24942	τ
Casein kinase II beta chain	3 5	IPI00013478.1	37808	Т
Cathepsin B	12	1 100000000	96171	
Cation-chloride cotransporter-interacting protein	811	F100024330.1		
	112	IP100012052.1	91941	
CD97	113	IP100019387.1	27860	
CDM_HUMAN	226	IP100005068.2	73296	
CDW92	119	IP100011631.1	88829	
	120	IP100018730.1	52118	1
Cerebral protein 10				1

CGBO HIMAN				
	29	IP100032827.1	14585	
	114	IP100008847.1	52917	T
[6-b)	115	IP100215921.1	57429	T
cholinergic receptor, nicotinic, alpha polypeptide 3	2 8	IP100007259.1	55637	T
Chondroitin sulfate proteoglycan 6	70	7 00 70000101		
CHRNA3	\$	IF100023102.1	141542	
Chromatin conceilio	116	IPI00027751.1	57310	T
Surging a subunit elongation factor FACT 140 kDa subunit	35	IPI00026970.1	119914	T
CNINAPI	227	IPI00219249.1	164756	$\neg \vdash$
COPINE FAMILY MEMBER.	281	IP100173232.1	61891	
	282	IP100024403.1	60131	
DAAM1	121	IP100000705 1	1949AE	
Dachshund 2	283	- C0C39000101	25000	
DAPK1	202	1.190005787.1	65323	
DC6 protein	122	IP100021250.1	160018	
DCTN1	36	IP100024620.1	11529	
Delta-1 catonin	192	IPI00011446.1	127404	
Dollar Carefull	284	IP100015202.1	104958	
Delia-o lany acid desaturase	193	IPI00003544.1	52259	
Della-like nomolog	298	IP100009191.1	41143	
Deoxyhypusine synthase	308	IP100026829 1	40971	
Dihydrofolate reductase	220	IDIOOOOOET 4	7,000	
Dkfzp586c1924	677	11100030357.1	28844	
	37	IP100031064.1	21527	

			07407	
	228 IF	1P100012033	37407	
	123 IF	P100217985.1	233103	
DOCK3	124 IF	IP100030770.1	32854	
	908	P100013802.2	44231	
Dynactin 2		IPI00023551.1	10922	
Dynein light chain 2A		DI00007675 1	56627	
		100007873.1	51157	
	12	F100009104.1	201.0	
	125	IP100106506.1	49148	 7
	40	IP100031552.2	39547	
	233	P100005707.3	166655	
Endocytic receptor Endo180		D100047E67 4	70578	
	230	F100017397.1	0.000	57
00000168820 (hypothetical protein with p-loop)	41	IP100151716.2	30//2	'
	194	IPI00102897.1	26308	
ENSG00000144840		10100100101	130960	ι –
ensp00000297280 (hypothetical protein with p-loop)	184	17100102036.1))	- 1
Eukaryotic translation initiation factor 4A, isoform	42	IP100025491.1	46154	- T
	231	IP100004047.1	82255	
EXIZ	232	IP100015135.1	104749	
EXTL3	406	IP100013161.1	78348	T
FACL1	150		97000	Т
C Z Y	195	[P[00031397.1	80340	Т
TACLS	196	IP100029737.1	79188	\neg
FACL4				

COB	13	IP100010843.1	77244	
Fe65L1	292	IP100023841.1	81080	T
Filamin, gamma	45	IDIO0165017 4	2000	T
FLJ10773	2	1.10010017.1	161182	
El Hagen	291	IPI00171198.1	52401	T
E 13040	234	IP100100927.1	56921	T
FI 143077	\$	IP100009707.1	43993	T
FI.120342	197	IPI00025520.1	53482	Τ
FI 120430	127	IP100015713.1	65084	T
E 190464	128	IP100015833.1	26152	T
1 CACAGO 1	198	IP100016418.1	47655	T
r L L L L L L L L L L L L L L L L L L L	199	IP100009343.1	17098	T
FLJ22555	120	1D10040900 4	17.100	٦
FLJ22678	2	11100103303.1	32545	-
FRAP1	130	IP100217885.1	85495	Τ
(Palarical and American Palarican Pa	44	IPI00031410.1	288892	T
m i	131	IP100014931.1	37062	T
GAP-associated tyrosine phosphoprotein p62	4	IP100008575.1	48227	_
GPR49	235	DI00004404 4	00000	Т
GTF2I	3	11 1000Z 1 13 1. 1	88888	
GTP-binding protein EBA	293	IPI00054042.1	112416	Τ-
HADH2/FBAB (mitochondria)	46	IP100026512.1	49098	\top
	47	IP100017726.1	26923	

		1 9868 1	55325	
HDACS	9		-	
	49	IP100005826.1	527472	
OZ protein	236	IP100005103.1	102368	
HK2 homolog of yeast golgi membrane protein yif1p (yip1p-interacting factor)	219	IPI00063544.1	33834	
7370007	20	IP100107156.1	28202	
40.076	51	IPI00107104.1	26057	
HSPC245	132	IP100001663.1	48841	
HTRA2	133	IP100163951.1	48771	·
HU-K4	133	IP100163951.1	48771	
HU-K4	2	IP100046057.1	68736	
Hunc18a	5	7 0000 0000 0000 0000 0000 0000 0000 0000	24406	ל -ר
UVPOTHETICAL PROTEIN	237	IP100164098.1	31103	79 —
The Control of the Company	238	IP100161721.1	94945	
Hypothetical protein (Fragment)	52	IP100018766.1	34095	
HYPOTHETICAL PROTEIN TESTOSTO				-
Hymothetical protein FLJ10795	55	IP100024779.1	138430	
HYPOTHETICAL PROTEIN FLJ12599.	53	IP100182757.1	102917	
11 Astronomy aratain El 114569	239	IP100161141.1	67283	 -
hypothetical protein a contract	56	IPI00101654.1	26305	
Hypothetical protein FLJZU397	135	IP100031005.1	40050	Γ-
Hypothetical protein FLJ23356	3	10000000	79799	1
Hypothetical protein FLJ23630	240	1.02650100141	13135	
Hypothetical protein KIAA0372	241	IP100005634.1	175486	\neg

Hypothetical protein KIAA0455	136	IP100160410.1	82983
	137	IP100013735.1	81463
nypotnetical protein MGC10924 similar to Nedd4 WW-binding protein 5	275	IP100012235.1	24899
hypothetical protein MCC13188		-	
	86	IP100031570.1	20713
HYPOTHETICAL BROTEIN SE 12000	276	IPI00172590.1	88020
CITICAL PROTEIN AP_1/4405.	134	IPI00159547.1	23035
ICAM-2	000		
IGF2R	200	IP100008477.1	30653
IKAD	242	IP100007226.1	274309
	22	IP100028877.1	150191
IL13HAZ	294	IP100032199.1	44176
Insulinoma-glucagonoma protein 20	58	IP100103536.1	183267
Integral membrane protein 2B (ITM2B)	16	IP100031821.1	30338
Integral membrane transporter protein	277	IP100020093.1	31735
IPI00104084 1			
ITPB1	15	IP100104084.1	36759
IIID-4	243	IP100036162.1	313945
KIAAOOEE	295	IP100023133.1	77524
KIA A OCES AFFIRE	29	IP100000899.1	169718
MINAGOOZ (FINAGIMEN!)	138	IP100014236.1	58417
	139	IP100160376.1	111759

	201 IF	IP100005680.1	93488	
	140	IP100014149.1	34833	
KIAAU103	09	IP100001458.1	250749	
KIAAU166	244	IP100010861.1	90027	
KIAAUZOI (FRAGINIENI)	61	IP100141330.2	532367	
KIAAUSZS (TRAGINEINT)	245	IP100004538.1	156999	
KIAA0363 (TRAGMENT)	62	IP100158296.2	214824	T
KIAA0564	83	IP100006669.1	94914	
KIAA0763	202	IP100021671.1	138688	
KIAA0922	246	P100007231.1	74536	
KIAA0971	1	DI00160387 1	121739	
KIAA1102 (Fragment)		F100100007.1	26970	-
KIAA1181 (FRAGMENT)	203	Piuuusess. i	6 1000	81
17. A 4 0 E O	247	IP100033429.1	19/211	
TIME A SECTION OF THE PROPERTY	204	IPI00001841.1	72964	
KIAA1533 (FRAGINIEN I)	299	IP100150950.1	62629	
KIAA1949	Ţ	IDIO0154267 1	37912	Τ-
Krab box protein ensp00000302970	2	IF 100104201.1	477E07	
I aminin gamma 1	65	IP100003386.1	70077	_
in the respect protein)	64	IP100057018.2	64414	
	248	IP100024531.1	179173	
LHP3	99	IP100009868.1	39236	
MBIP	67	IP100023954.2	175609	Γ-
MEGF7 (FRAGMENT)	040	IPI00012202 1	36724	1
MEP50	010			٦

Masanchymal atom call and in Social				
moseriary and sterr cell protein DSCD75	205	IPI00010292.1	23865	
MGC2803	286	IDI00034506 4	07707	
MGC4022	3	11100031326.1	91481	
	90 90	IP100010625.1	59797	
WGC4248	141	IP100031582 1	A76A6	
MGC5442	1/10	, 9EEE 0000101		
MT-ACT48	74.1	IF1000277/3.1	26261	
Myosin IXB	89	IPI00032410.1	46355	
NAP-1 related protein	69	IP100003064.1	228624	_
NET 1	301	IP100155244.1	44159	
Normalia	20	IP100029817.1	45467	
	73	IP100006314.1	161883	
Neurocalcin delta	302	IPI00140719 1	20444	
Neurotrypsin		1.21 12	41177	
Nicastrin	506	IP100011063.1	97012	
	147	IP100021983.1	78411	
MIDENABI	143	IP100032413.1	28779	
NIPSNIADO	71	IP100021086.2	33310	
Z-IVIO IIVI	72	IP100016077.1	33743	
	144	IP100005107.1	142149	
	145	IP100152981.1	68760	
INFICA, a component of the nuclear pore complex	146	IP100001676.1	73788	
NRP2				
	249	IPI00029693.1	104831	

Nuclear receptor co-repressor/HDAC3 complex subunit TBLR1	311	IP100002922.2	55595
	148	IDIO0141318 1	86022
teiri	9-	17100141316.1	20025
Paladin	77	IP100161782.1	96754
PAS domain containing serine/threonine kinase	207	IP100141040.1	142859
PCDHA10	250	IP100001513.1	102875
PCDHB12	251	IP100001450.1	86770
PCDHB13: protocadherin beta 13	252	IP100001449.1	87552
Pcdhb17	258	IP100045942.1	64852
PCDHB4	253	IP100001429.1	87270
PCDHGB1	254	IP100003890.1	100360
PCDHGB6	255	IP100003897.1	101043
PDZ and LIM domain protein 1	74	IP100010414.2	36072
PDZ domain protein MAGI-3	18	IP100022491.1	111914
Pen-2	209	IP100020516.1	12029
Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	78	IP100004383.1	70637
PILB	75	IP100032871.1	21468
PILT	92	IP100010544.2	60705
PMPCB	256	IP100025726.1	54168
PP1, regulatory subunit 15B	208	IP100045837.1	79125
PP2C gamma	257	IP100006167.1	59272

PPP2CA (PP2A, catalytic subunit, alpha)	312	IPIODOR380 1	35504
			1
rrrzob (rrza, catalytic subunit, beta)	313	IP100003461.1	35575
PPP2R1A (PP2A, 65 KDA regulatory subunit A, alpha)	314	IP100025326.1	65092
PPP2RBA, (PP2A, 55 KDA regulatory subunit B, alpha)	19	IP100220836.1	55642
Presenilin-1	210	IP100026333.1	52163
Presenilin-2	172	IP100028485.1	50140
Procollagen C-endopeptidase enhancer	79	IP100014828.1	47972
Programmed cell death 10	80	IP100026997.1	24658
Prohibitin	173	IPI00017334.1	29804
Protein amplified in osteosarcoma (OS-9)	211	IPI00013268.1	75562
Protein similar to AGCP6688		1D100140700 4	14000
Protein similar to probable mitotic centromere associated kinesin	5 6	1 100 140 703. I	14290
	2	IF100088667.1	18400
Protein similar to stromal cell-derived factor 2	212	IP100034198.1	23026
Protocadherin 7	259	IP100001893.2	116105
Protocadherin beta 16	260	IP100016595.1	84936
Protocadherin beta 8	213	IP100009033.1	87624
PSMA1	149	IP100016832.1	29556
PSMA3	150	IP100016834.1	28302

152 IPI00029623.1 153 IPI00028006.1 154 IPI00028006.1 155 IPI00028006.1 156 IPI00028006.1 157 IPI00219629.1 158 IPI00011126.2 160 IPI00018398.2 161 IPI00018398.2 162 IPI00018398.2 163 IPI00018398.2 164 IPI00018398.1 165 IPI00015333.1 166 IPI00015333.1 167 IPI00015588.1 168 IPI00012268.1 170 IPI00012268.1 171 IPI00022694.1	PSMA4	151	IP100016836.1	29484
153 IPIO0028006.1 154 IPIO0028006.1 155 IPIO0028006.1 156 IPIO0020806.1 157 IPIO0219629.1 158 IPIO0011126.2 160 IPIO0018398.2 161 IPIO0018398.2 162 IPIO0018398.2 163 IPIO0023919.2 164 IPIO0023919.2 165 IPIO0018398.1 166 IPIO0018398.1 167 IPIO0015598.1 168 IPIO0003569.1 169 IPIO0012268.1 170 IPIO0022694.1 171 IPIO0022694.1	PSMA6	152	1P100029623.1	27399
154 IPI00028006.1 155 IPI00028004.2 156 IPI000219629.1 157 IPI00219629.1 158 IPI00011126.2 159 IPI00014358.2 160 IPI00013398.2 161 IPI00013398.2 162 IPI00013398.2 163 IPI00013398.2 164 IPI00021926.2 165 IPI00015333.1 166 IPI00015333.1 167 IPI00003569.1 168 IPI00012268.1 169 IPI00012269.1 170 IPI0002269.4.1	PSMB1	153	IP100025019.1	26489
155 IP100028004.2 156 IP100000806.1 157 IP100219629.1 158 IP100011126.2 159 IP100011126.2 161 IP100018398.2 162 IP100020042.2 163 IP100023919.2 164 IP100021926.2 165 IP100015333.1 166 IP100015338.1 167 IP100003569.1 169 IP100012268.1 170 IP10001268.1 171 IP100022694.1	PSMB2 .	154	IP100028006.1	22836
156	PSMB3	155	IP100028004.2	22949
157 IPI00219629.1 158 IPI00000811.2 159 IPI00011126.2 160 IPI0001435.1 161 IPI00018398.2 162 IPI0002042.2 163 IPI00023919.2 164 IPI00021926.2 165 IPI00015333.1 166 IPI00015598.1 167 IPI00003569.1 169 IPI00012268.1 170 IPI00012694.1	PSMB4	156	IP100000806.1	29192
158 IP10000811.2 159 IP100011126.2 160 IP100021435.1 161 IP100018398.2 162 IP100020042.2 163 IP100023919.2 164 IP100023919.2 165 IP100015333.1 165 IP100015333.1 166 IP100015333.1 167 IP100003569.1 169 IP100012268.1 170 IP100012268.1 171 IP100022694.1 171 IP100022694.1 171 IP100022694.1 172 IP100022694.1 173 IP100022694.1 174 IP100022694.1 175	PSMB5	157	IPI00219629.1	28480
159 IPI00011126.2 160 IPI00021435.1 161 IPI00021435.1 162 IPI00020042.2 163 IPI00023919.2 164 IPI00023919.2 165 IPI00023919.2 165 IPI00015333.1 165 IPI00015333.1 165 IPI00015333.1 167 IPI00003569.1 168 IPI00003569.1 169 IPI00012268.1 170 IPI00012268.1 171 IPI00022694.1 IPI00022	PSMB6	158	IP100000811.2	25358
160 IPI00021435.1 161 IPI00018398.2 162 IPI00023919.2 163 IPI00023919.2 164 IPI00021926.2 165 IPI0001533.1 166 IPI00105598.1 167 IPI00003569.1 169 IPI00012268.1 170 IPI00012268.1 171 IPI00022694.1	PSMC1	159	IPI00011126.2	49185
161 IPI00018398.2 162 IPI00020042.2 163 IPI00023919.2 164 IPI00023919.2 165 IPI0001533.1 166 IPI0001533.1 167 IPI0000359.1 168 IPI00003569.1 169 IPI00012268.1 170 IPI00011603.2 171 IPI00022694.1	PSMC2	160	IPI00021435.1	48634
162 IP100020042.2 163 IP100023919.2 164 IP100021926.2 165 IP100015333.1 166 IP100105598.1 167 IP100003569.1 168 IP100003569.1 169 IP100012268.1 170 IP100011603.2 171 IP100022694.1	PSMC3	161	IPI00018398.2	49204
163 IPI00023919.2 164 IPI00021926.2 165 IPI0001533.1 166 IPI00015598.1 167 IPI00003569.1 168 IPI00003569.1 169 IPI00012268.1 170 IPI00011603.2 171 IPI00022694.1	PSMC4	162	IP100020042.2	47366
164 IPI00021926.2 165 IPI00015333.1 166 IPI00105598.1 167 IPI00003569.1 168 IPI00003570.1 169 IPI00012268.1 170 IPI00011603.2 171 IPI00022694.1	PSMC5	163	IP100023919.2	45626
165 IPI00015333.1 166 IPI00105598.1 167 IPI00003569.1 168 IPI00003570.1 169 IPI00012268.1 170 IPI00011603.2 171 IPI00022694.1	PSMC6	164	IP100021926.2	44173
166 IP100105598.1 167 IP100003569.1 168 IP100003570.1 169 IP100012268.1 170 IP100011603.2 171 IP100022694.1	PSMD1	165	IP100015333.1	105866
167 IP100003569.1 3 168 IP100003570.1 169 IP100012268.1 170 IP100011603.2 171 IP100022694.1	PSIMD11	166	IP100105598.1	47464
3 168 IP100003570.1 4 169 IP100012268.1 5 170 IP100011603.2 171 IP100022694.1	PSMD12	167	IP100003569.1	52904
169 IP100012268.1 170 IP100011603.2 171 IP100022694.1	PSMD13	168	IP100003570.1	42945
170 IPI00011603.2 171 IPI00022694.1	PSMD2	169	IP100012268.1	100200
171 IPI00022694.1	PSMD3	170	IPI00011603.2	60978
	PSMD4	171	IP100022694.1	40737
261 (PI00014577.1	RAB-18	261	IP100014577.1	22977

Baha GTPaca activating protein				
ase activating protein, non-catalytic subunit	263	IP100018280.3	155985	
RAB7L1	8			
BANBP1	82	IP100024775.1	23155	
Roolin	83	IP100018856.1	23310	T
DEBO	88	IP100021018.1	388402	
nero piotein	214	IP100010353.1	30541	$\neg \neg$
HEST corepressor	303	IP100008531.1	53028	\neg
Hetinal short-chain dehydrogenase/reductase retSDR2	216	IP100008260.1	32964	
RING finger protein 5	215	IPINON19808 4	10004	
RNASEL	262	IPION1E864 1	19001	
RNB6	24	1. 1000 13004. I	93333	
RPGR-interacting protein 1	13	IF100008862.1	44792	
RPS6KA3	40	IP100044777.1	103123	
S-100 alpha	174	IP100020898.1	83736	
S-100 heta	296	IPI00010824.1	10415	
	304	IPI00220413.1	10713	
	22	IPI00017341.2	49256	
line protein phosphatase 6	06	IP100012970.1	35144	
Sideroflexin 1	266	IDIOOOOOO	01010	
Signal transducer and activator of transcrintion-1	3	וו וספספספספיב	81905	
	/97	IP100030781.1	87335	
	268	IP100007052.1	16980	

SIMILAR TO GAMMA INTERFERON INDUCIBLE GENE IP10.	175	IP100058185.3	95055	
similar to SD27354p [Drosophila melanogaster]	66	IP100103057.1	13291	
	264	IP100072534.1	103077	
	98	IP100010470.1	23315	
	177	IPI00016022.1	92100	
	91	IP100022608.1	248441	
slated receptor	265	IP100005751.1	62924	
SPTLC2	178	IP100100476.1	41523	
Stearoyl-CoA desaturase	260	IPI00007919.1	75337	
Sterile alpha and HEAT/Armadillo motif protein	3			
	270	IP100019898.1	64763	587
Sterol O-acyltransferase	87	IPI00021199.2	21017	,
STMN3	176	IP100154566.1	73533	
STRA6 isoform 1	24.7	101001066422	23511	т—
Stromal cell-derived factor 2-like 1	717	F 00000011	22023	
STYIA	88	1P100003370.1	23050	- T-
	88	IP100021996.2	50331	
SUCLAZ	35	IPI00013947.1	24555	
Synaptogyrin 3	315	IP100025499.1	45850	
Таи	820	IP100022748.2	26538	_
tegt: testis enhanced gene transcript (bax inhibitor 1)	0/2			
Thioredoxin domain-containing protein	218	IP100001028.1	32535	

TNDCAR				
	287	IPI00160501.1	127290	
I pari	179	IP100102213 1		T
TPST1	900	7 000000101	Opero	-
Transcription factor CP2	007	11-100030106.1	42188	
Tiple functional domain	23	IPI00037599.1	57256	1 -
inple full cuorda domain protein (PTPRF interacting)	271	IP100026676.1	324106	
TYK2	83	IDIOO000E0 1	400600	
tyrosine phosphatase enso00000149185		II IOOOEEOOO. I	000001	
	220	IP100102935.1	22844	1
Ubiquitin-protein ligase E3-alpha	9	7 00001700101		
Ubjauitin-protein ligase EDD	† 5	IP100156938.1	83595	
	180	IP100026320.1	309352	
	272	IP100021472.1	103102	
vacuolar ATP synthase membrane sector associated protein m8-9	273	IP100041030.1	39036	
Vacuolar profein sorting profein 19		-		
VGE nerve prough factor industrial	279	IP100060946.1	64959	
Service actor madeline protein	92	IP100019628.1	67287	
Voltage-dependent anion channel 2	Ş			
Wolframin	<u> </u>	IP:100019625.1	31595	
Vithoio	182	IPI00008711.1	100306	
A libera	96	IP100017817.1	82512	
X11beta	96	IP100017817 1	00510	
Y391_HUMAN			71670	
oin 108	274	IP100004584.1	65486	
Zinc finger protein 227	97	IP100032608.2	154911	
	24	IPI00220069.1	56818	

IP100015213.1 ZIP kinase

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BIOCHEMICAL ACTIVITIES OF THE COMPLEXES

TABLE 3

	Regulator of APP processing and APP function
x i nera-complex	Regulator of APP processing and APP function
PSEN2-complex	Gamma-secretase complex
Nicastrin-complex (Gamma-secretase activity and assembly (trafficking)
Aph-1a-complex (Gamma-secretase activity and assembly (trafficking)
Pen-2-complex (Gamma-secretase activity and assembly (trafficking)
APP695SW-complex	Signalling activity (regulator of transcription)
APP-C99-complex	Signalling activity (regulator of transcription)
Tau-complex F	Regulator of microtubules and vesicle transport along microtubules
APP695SW S	Signalling activity (regulator of transcription)

TABLE 4

MEDICAL APPLICATIONS OF THE COMPLEXES

Complex	Medical application Medical application
Fe65-complex	neurodegenerative disease such as Alzheimer's disease, illinariancy disease cancer and breast disorders, rheumatoid arthritis and inflammatory bowel disease; cancer such as prostate cancer and breast cancer and skin cancer
X11b-complex	neurodegenerative disease such as Alzheimer's disease; inflammatory conditions such as ulcerative colitis, Crohn's disease and artherosclerosis
PSEN2-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Nicastrin- complex	neurodegenerative diseases such as Alzheliner s disease and remove the second s
App. 19-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative disorders
Aprila compros	
Pen-2-complex	neurodegenerative discussional and related neurodegenerative disorders
APP695SW-complex	neurodegenerative diseases such as Alzheimei s disease and remodegenerative disease such as Alzheimei s disease and remodegenerative
	neurodenenative diseases such as Alzheimer's disease and related neurodegenerative disorders
APP-C99- complex	ileurode de la contraction de
Tau-complex	neurodegenerative diseases such as Alzheimer's disease and related neurodegenerative diseases

CLAIMS

- 1. A protein complex selected from complex (I) and comprising (a) at least one first protein, which first protein is selected from the group of proteins in table 1, fourth column of a given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof, or a variant of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions; and (b) at least one second protein, which second protein is selected from the group of proteins in table 1, fifth column of said given complex, or a functionally active derivative thereof, or a functionally active fragment thereof, or a homologue thereof. or a variant of said second protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions: and a complex (II) comprising at least two of said second proteins. wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCI (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 2. A protein complex comprising a first protein selected from the proteins listed in table 1, fourth column of a given complex or a homologue or variant thereof, or a functionally active fragment or functionally active derivative of said first protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said first protein under low stringency conditions, and at least one second protein selected from the group of proteins in table 1, fifth column of a given complex, or a variant or homologue thereof, or a functionally active fragment or a functionally active derivative of said second protein, the variant of said second protein being encoded by a nucleic acid that hybridizes to the nucleic acid of said second protein under low-stringency conditions, and wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% BSA, 100 ug/ml denatured salmon sperm

DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4) 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

- 3. A protein complex comprising all proteins selected from the proteins in table 1, third column of a given complex or at least one protein being a homologue thereof, or a variant thereof or functionally active fragment or functionally active derivative of said protein, said variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low stringency conditions; wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.
- 4. A protein complex that comprises all proteins as listed in table 1, third column for a given complex or at least one protein being a homologue or a variant thereof, or a functionally active fragment or a functionally active derivative thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of any of said proteins under low stringency conditions, except at least one protein of the proteins listed in table 5, third column, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1-5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C, with the provisio that the complex comprises at least one protein selected from table 1, fifth column of a given complex.

- 5. The complex of any of Claim 1 4 comprising at least one functionally active derivative of said first protein and/or a functionally active derivative of said second protein, wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an amino acid sequence different from the first protein or second protein.
- 6. The complex of Claim 5 wherein the functionally active derivative is a fusion protein comprising said first protein or said second protein fused to an affinity tag or label.
- 7. The complex of any of Claim 1 4 comprising a fragment of said first protein and/or a fragment of said second protein, which fragment binds to another protein component of said complex.
- 8. The complex of any of Claim 1 7 that is involved in at least one biochemical activity as stated in table 3.
- 9. A process for preparing a complex of any of Claim 1 8 and optionally the components thereof comprising the following steps: expressing a protein of the complex, preferably a tagged protein, in a target cell, or a tissue or an organ, isolating the protein complex which is attached to the protein, preferably the tagged protein, and optionally disassociating the protein complex and isolating the individual complex members.
- 10. The process according to Claim 9 wherein the tagged protein comprises two different tags which allow two separate affinity purification steps.
- 11. The process according to any of Claim 9 10 wherein the two tags are separated by a cleavage site for a protease.
- 12. Component of a protein complex obtainable by a process according to any of Claim 9- 11.
- 13. Protein selected from the group of proteins in table 1, sixth column of a given complex or a homologue or a variant of thereof, or a functionally active fragment or a

functionally active derivative of said protein, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid encoding said protein under low stringency conditions, wherein said low stringency conditions comprise hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 ug/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40°C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55°C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60°C.

- 14. Nucleic acid encoding a protein according to Claim 13.
- 15. Construct, preferably a vector construct, comprising
 - (a) a nucleic acid according to Claim 14 and at least one further nucleic acid which is normally not associated with said nucleic acid, or
 - (b) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, at least one of said proteins being selected from the first group of proteins according to Claim 1 (a) and at least one of said proteins, being selected from the second group of proteins according to Claim 1 (b) or
 - (c) at least two separate nucleic acid sequences each encoding a different protein, or a functionally active fragment or a functionally active derivative thereof, or a homologue or a variant thereof, said proteins being selected from the proteins of complex (II) according to Claim 1.
- 16. Host cell, containing a vector comprising at least one nucleic acid of Claim 14 and /or a construct of Claim 15 or containing several vectors each comprising at least one nucleic acid encoding at least one protein selected from the first group of proteins according to Claim 1 (a) and at least one nucleic acid encoding at least one protein selected from the second group of proteins according to Claim 1 (b).
- 17. An antibody or a fragment of said antibody containing the binding domain thereof, selected from an antibody or fragment thereof, which binds the complex of any of

Claim 1 - 8 and which does not bind any of the proteins of said complex when uncomplexed and an antibody or a fragment of said antibody containing the binding demain thereof which binds to any of the proteins of the group of proteins according to Claim 13.

- 18. A kit comprising in one or more containers:
 - (a) the complex of any of Claim 1 8 and/or the proteins of Claim 13 and/or
 - --(b)-an-antibody-according-to-Claim 17 and/or
 - (c) a nucleic acid encoding a protein of the complex of any of Claim 1 8 and/or a protein of Claim 13 and/or
 - (d) cells expressing the complex of any of Claim 1 8 and/or a protein of Claim 13 and, optionally,
 - (e) further components such as reagents, buffers and working instructions.
- 19. The kit according to Claim 18 for processing a substrate of a complex of any one of Claim 1 8.
- 20. The kit according to Claim 18 for the diagnosis or prognosis of a disease or a disease risk, preferentially for a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 21. Array, preferably a microarray, in which at least a complex according to any of Claim 1 8 and/or at least one protein according to Claim 13 and/or at least one antibody according to Claim 17 is attached to a solid carrier.
- 22. A process for modifying a substrate of a complex of any one of Claim 1 8 comprising the step of bringing into contact a complex of any of Claim 1 8 with said substrate, such that said substrate is modified.
- 23. A pharmaceutical composition comprising the protein complex of any of Claim 1 8 and/or a protein according to Claim 13.

- 24. A pharmaceutical composition according to Claim 23 for the treatment of diseases and disorders, preferentially for diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 25. A method for screening for a molecule that binds to a complex of any one of Claim 1 8 and/or a protein of Claim 13, comprising the following steps:
 - (a) exposing said complex or protein, or a cell or organism containing said complex or said protein, to one or more candidate molecules; and
 - (b) determining whether said candidate molecule is bound to the complex or protein.
- 26. A method for screening for a molecule that modulates directly or indirectly the function, activity, composition or formation of a complex of any one of Claim 1 8 comprising the steps of:
 - (a) exposing said complex, or a cell or organism containing said complex to one or more candidate molecules; and
 - (b) determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent upon the function of the complex and/or product of a gene dependent on the complex in the presence of the one or more candidate molecules, wherein a change in said amount, activity, protein components or intracellular localization relative to said amount, activity, protein components and/or intracellular localization and/or a change in the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in the absence of said candidate molecules indicates that the molecule modulates function, activity, or composition of said complex.
- 27. The method of Claim 26, wherein the amount of said complex is determined.
- 28. The method of Claim 26, wherein the activity of said complex is determined.

- 29. The method of Claim 28, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 30. The method of Claim 26, wherein the amount of the individual protein components of said complex is determined.
- 31. The method of Claim 30, wherein said determining step comprises determining whether any of the proteins listed in table 1, third column of said complex, or a functionally active fragment or a functionally active derivative thereof, or a variant or a homologue thereof, the variant being encoded by a nucleic acid that hybridizes to the nucleic acid of said protein under low-stringency conditions, is present in the complex.
- 32. The method of any of Claim 26 31, wherein said method is a method of screening for a drug for treatment or prevention of a disease or disorder, preferentially of a disease or disorder selected from the diseases or disorders such as those as stated in column 2, table 4 of a given complex.
- 33. Use of a molecule that modulates the amount of, activity of, or the protein components of the complex of any one of Claim 1 8 for the manufacture of a medicament for the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as those as stated in column 2, table 4 of a given complex.
- 34. A method for the production of a pharmaceutical composition comprising carrying out the method of Claim 26 31 to identify a molecule that modulates the function, activity, composition or formation of said complex, and further comprising mixing the identified molecule with a pharmaceutically acceptable carrier.

- 35. A method for diagnosing or screening for the presence of a disease or disorder or a predisposition for developing a disease or disorder in a subject, which disease or disorder is characterized by an aberrant amount of, component disposition of, or intracellular localization of the complex of any one of the Claim 1 8, comprising determining the amount of, activity of, protein components of, and/or intracellular localization of, said complex and/or the transcription level of a gene regulated by the complex and/or the abundance and/or activity of a protein or protein complex dependent on the function of the complex and/or product of a gene dependent on the complex in a comparative sample derived from a subject, wherein a difference in said amount, activity, or protein components of, said complex in a corresponding sample from a subject not having the disease or disorder or predisposition indicated the presence in the subject of the disease or disorder or predisposition in the subject.
- 36. The method of Claim 35, wherein the amount of said complex is determined.
- 37. The method of Claim 35, wherein the activity of said complex is determined.
- 38. The method of Claim 37, wherein said determining step comprises isolating from the cell or organism said complex to produce said isolated complex and contacting said isolated complex in the presence or absence of a candidate molecule with a substrate of said complex and determining whether said substrate is processed in the absence of the candidate molecule and whether the processing of said substrate is modified in the presence of said candidate molecule.
- 39. The method of Claim 35, wherein the amount of the individual protein components of said complex is determined.
- 40. The method of Claim 39, wherein said determining step comprises determining whether any of the proteins according to Claim 13 is present in the complex.
- 41. The complex of any one of Claim 1 8, or a protein of Claim 13 or an antibody or fragment thereof of Claim 17, for use in a method of diagnosing a disease or disorder, preferentially of a disease or disorder such as neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

- 42. A method for treating or preventing a disease or disorder characterized by an aberrant amount of, activity of, component composition of or intracellular localization of, the complex of any one of Claim 1 8, comprising administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more molecules that modulate the amount of, activity of, or protein composition of, said complex.
- 43. The method according to Claim 42, wherein said disease or disorder involves decreased levels of the amount or activity of said complex.
- 44. The method according to Claim 42, wherein said disease or disorder involves increased levels of the amount or activity of said complex.
- 45. Complex of Claim 1 8 and/or a protein as listed in table 1, fifth column of said complex as a target for an active agent of a pharmaceutical, preferably a drug target, in the treatment or prevention of a disease or disorder, preferentially of a disease or disorder such as a neurodegenerative disease such as those as stated in column 2, table 4 of a given complex.

SEQUENCES

SEQID No:1

MDDREDLVYQAKLAEQAERYDEMVESMKKVAGMDVELTVEERNLLSVAYKNVIGARR ASWRIISSIEQKEENKGGEDKLKMIREYRQMVETELKLICCDILDVLDKHLIPAANTGESK VFYYKMKGDYHRYLAEFATGNDRKEAAENSLVAYKAASDIAMTELPPTHPIRLGLALNF SVFYYEILNSPDRACRLAKAAFDDAIAELDTLSEESYKDSTLIMQLLRDNLTLWTSDMQG DGEEQNKEALQDVEDENQ

SEQID No:2

MTMDKSELVQKAKLAEQAERYDDMAAAMKAVTEQGHELSNEERNLLSVAYKNVVGAR RSSWRVISSIEQKTERNEKKQQMGKEYREKIEAELQDICNDVLELLDKYLIPNATQPESK VFYLKMKGDYFRYLSEVASGDNKQTTVSNSQQAYQEAFEISKKEMQPTHPIRLGLALNF SVFYYEILNSPEKACSLAKTAFDEAIAELDTLNEESYKDSTLIMQLLRDNLTLWTSENQG DEGDAGEGEN

SEQID No:3

MGDREQLLQRARLAEQAERYDDMASAMKAVTELNEPLSNEDRNLLSVAYKNVVGARR SSWRVISSIEQKTMADGNEKKLEKVKAYREKIEKELETVCNDVLSLLDKFLIKNCNDFQY ESKVFYLKMKGDYYRYLAEVASGEKKNSVVEASEAAYKEAFEISKEQMQPTHPIRLGLA LNFSVFYYEIQNAPEQACLLAKQAFDDAIAELDTLNEDSYKDSTLIMQLLRDNLTLWTSD QQDEEAGEGN

SEQID No:4

MVDREQLVQKARLAEQAERYDDMAAAMKNVTELNEPLSNEERNLLSVAYKNVVGARR SSWRVISSIEQKTSADGNEKKIEMVRAYREKIEKELEAVCQDVLSLLDNYLIKNCSETQY ESKVFYLKMKGDYYRYLAEVATGEKRATVVESSEKAYSEAHEISKEHMQPTHPIRLGLA LNYSVFYYEIQNAPEQACHLAKTAFDDAIAELDTLNEDSYKDSTLIMQLLRDNLTLWTSD QQDDDGGEGNN

SEQID No:5

MEKTELIQKAKLAEQAERYDDMATCMKAVTEQGAELSNEERNLLSVAYKNVVGGRRSA WRVISSIEQKTDTSDKKLQLIKDYREKVESELRSICTTVLELLDKYLIANATNPESKVFYLK MKGDYFRYLAEVACGDDRKQTIDNSQGAYQEAFDISKKEMQPTHPIRLGLALNFSVFYY EILNNPELACTLAKTAFDEAIAELDTLNEDSYKDSTLIMQLLRDNLTLWTSDSAGEECDA AEGAEN

SEQID No:6

MDKNELVQKAKLAEQAERYDDMAACMKSVTEQGAELSNEERNLLSVAYKNVVGARRS SWRVVSSIEQKTEGAEKKQQMAREYREKIETELRDICNDVLSLLEKFLIPNASQAESKVF YLKMKGDYYRYLAEVAAGDDKKGIVDQSQQAYQEAFEISKKEMQPTHPIRLGLALNFSV FYYEILNSPEKACSLAKTAFDEAIAELDTLSEESYKDSTLIMQLLRDNLTLWTSDTQGDEA EAGEGGEN

SEQID No:7

MGPASPAARGLSRRPGQPPLPLLLPLLLLLLRAQPAIGSLAGGSPGAAEAPGSAQVAGL CGRLTLHRDLRTGRWEPDPQRSRRCLRDPQRVLEYCRQMYPELQIARVEQATQAIPM ERWCGGSRSGSCAHPHHQVVPFRCLPGEFVSEALLVPEGCRFLHQERMDQCESSTR RHQEAQEACSSQGLILHGSGMLLPCGSDRFRGVEYVCCPPPGTPDPSGTAVGDPSTR SWPPGSRVEGAEDEEEESFPQPVDDYFVEPPQAEEEEETVPPPSSHTLAVVGKVTPT PRPTDGVDIYFGMPGEISEHEGFLRAKMDLEERRMRQINEVMREWAMADNQSKNLPK ADRQALNEHFQSILQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQADPP QAERVLLALRRYLRAEQKEQRHTLRHYQHVAAVDPEKAQQMRFQVHTHLQVIEERVN QSLGLLDQNPHLAQELRPQIQELLHSEHLGPSELEAPAPGGSSEDKGGLQPPDSKDDT PMTLPKGSTEQDAASPEKEKMNPLEQYERKVNASVPRGFPFHSSEIQRDELAPAGTGV SREAVSGLLIMGAGGGSLIVLSMLLLRRKKPYGAISHGVVEVDPMLTLEEQQLRELQRH GYENPTYRFLEERP

SEQID No:8

MAATGTAAAAATGRLLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLN MHVNIQTGKWEPDPTGTKSCFETKEEVLQYCQEMYPELQITNVMEANQRVSIDNWCR RDKKQCKSRFVTPFKCLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEAC LTQGMTLYSYGMLLPCGVDQFHGTEYVCCPQTKIIGSVSKEEEEEDEEEEEDEEED YDVYKSEFPTEADLEDFTEAAVDEDDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTE PGSDGTMSDKEITHDVKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNR NNFESEDYCMAVCKAMIPPTPLPTNDVDVYFETSADDNEHARFQKAKEQLEIRHRNRM DRVKKEWEEAELQAKNLPKAERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAM LNDRRRMALENYLAALQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKA

AQMKSQVMTHLHVIEERRNQSLSLLYKVPYVAQEIQEEIDELLQEQRADMDQFTASISE TPVDVRVSSEESEIPPFHPFHPFPALPENEDTQPELYHPMKKGSGVGEQDGGLIGAE EKVINSKNKVDENMVIDETLDVKEMIFNAERVGGLEEERESVGPLREDFSLSSSALIGLL VIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHGYENPTYKYLEQ MQI

SEQID No:9

MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPS
GTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR
CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPC
GIDKFRGVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEE
EEVAEVEEEEADDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVREV
CSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAMS
QSLLKTTQEPLARDPVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRER
MSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVE
AMLNDRRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDP
KKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLAN
MISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSVPANTENEVE
PVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS
NKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGY
ENPTYKFFEQMQN

SEQID No:10

MDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSI HHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

SEQID No:11

MALLAMHSWRWAAAAAAFEKRRHSAILIRPLVSVSGSGPQWRPHQLGALGTARAYQIP ESLKSITWQRLGKGNSGQFLDAAKALQVWPLIEKRTCWHGHAGGGLHTDPKEGLKDV DTRKIIKAMLSYVWPKDRPDLRARVAISLGFLGGAKAMNIVVPFMFKYAVDSLNQMSGN MLNLSDAPNTVATMATAVLIGYGVSRAGAAFFNEVRNAVFGKVAQNSIRRIAKNVFLHL HNLDLGFHLSRQTGALSKAIDRGTRGISFVLSALVFNLLPIMFEVMLVSGVLYYKCGAQF ALVTLGTLGTYTAFTVAVTRWRTRFRIEMNKADNDAGNAAIDSLLNYETVKYFNNERYE AQRYDGFLKTYETASLKSTSTLAMLNFGQSAIFSVGLTAIMVLASQGIVAGTLTVGDLVM

VNGLLFQLSLPLNFLGTVYRETRQALIDMNTLFTLLKVDTQIKDKVMASPLQITPQTATVA FDNVHFEYIEGQKVLSGISFEVPAGKKVAIVGGSGSGKSTIVRLLFRFYEPQKGSIYLAG QNIQDVSLESLRRAVGVVPQDAVLFHNTIYYNLLYGNISASPEEVYAVAKLAGLHDAILR MPHGYDTQVGERGLKLSGGEKQRVAIARAILKDPPVILYDEATSSLDSITEETILGAMKD VVKHRTSIFIAHRLSTVVDADEIIVLDQGKVAERGTHHGLLANPHSIYSEMWHTQSSRVQ NHDNPKWEAKKENISKEEERKKLQEEIVNSVKGCGNCSC

SEQID No:12

MATVTATTKVPEIRDVTRIERIGAHSHIRGLGLDDALEPRQASQGMVGQLAARRAAGVV LEMIREGKIAGRAVLIAGQPGTGKTAIAMGMAQALGPDTPFTAIAGSEIFSLEMSKTEALT QAFRRSIGVRIKEETEIIEGEVVEIQIDRPATGTGSKVGKLTLKTTEMETIYDLGTKMIESL TKDKVQAGDVITIDKATGKISKLGRSFTRARDYDAMGSQTKFVQCPDGELQKRKEVVHT VSLHEIDVINSRTQGFLALFSGDTGEIKSEVREQINAKVAEWREEGKAEIIPGVLFIDEVH MLDIESFSFLNRALESDMAPVLIMATNRGITRIRGTSYQSPHGIPIDLLDRLLIVSTTPYSE KDTKQILRIRCEEEDVEMSEDAYTVLTRIGLETSLRYAIQLITAASLVCRKRKGTEVQVDD IKRVYSLFLDESRSTQYMKEYQDAFLFNELKGETMDTS

SEQID No:13

MSVPSSLSQSAINANSHGGPALSLPLPLHAAHNQLLNAKLQATAVGPKDLRSAMGEGG GPEPGPANAKWLKEGQNQLRRAATAHRDQNRNVTLTLAEEASQEPEMAPLGPKGLIHL YSELELSAHNAANRGLRGPGLIISTQEQGPDEGEEKAAGEAEEEEEDDDDEEEEEDLS SPPGLPEPLESVEAPPRPQALTDGPREHSKSASLLFGMRNSAASDEDSSWATLSQGSP SYGSPEDTDSFWNPNAFETDSDLPAGWMRVQDTSGTYYWHIPTGTTQWEPPGRASP SQGSSPQEESQLTWTGFAHGEGFEDGEFWKDEPSDEAPMELGLKEPEEGTLTFPAQS LSPEPLPQEEEKLPPRNTNPGIKCFAVRSLGWVEMTEEELAPGRSSVAVNNCIRQLSYH KNNLHDPMSGGWGEGKDLLLQLEDETLKLVEPQSQALLHAQPIISIRVWGVGRDSGRE RDFAYVARDKLTQMLKCHVFRCEAPAKNIATSLHEICSKIMAERRNARCLVNGLSLDHS KLVDVPFQVEFPAPKNELVQKFQVYYLGNVPVAKPVGVDVINGALESVLSSSSREQWT PSHVSVAPATLTILHQQTEAVLGECRVRFLSFLAVGRDVHTFAFIMAAGPASFCCHMFW CEPNAASLSEAVQAACMLRYQKCLDARSQASTSCLPAPPAESVARRVGWTVRRGVQS LWGSLKPKRLGAHTP

SEQID No:14

MQRRDDPAARMSRSSGRSGSMDPSGAHPSVRQTPSRQPPLPHRSRGGGGGSRGGA

RASPATQPPPLLPPSATGPDATVGGPAPTPLLPPSATASVKMEPENKYLPELMAEKDSL DPSFTHAMQLLTAEIEKIQKGDSKKDDEENYLDLFSHKNMKLKERVLIPVKQYPKFNFVG KILGPQGNTIKRLQEETGAKISVLGKGSMRDKAKEEELRKGGDPKYAHLNMDLHVFIEV FGPPCEAYALMAHAMEEVKKFLVPDMMDDICQEQFLELSYLNGVPEPSRGRGVPVRG RGAAPPPPPVPRGRGVGPPRGALVRGTPVRGAITRGATVTRGVPPPPTVRGAPAPRA RTAGIQRIPLPPPPAPETYEEYGYDDTYAEQSYEGYEGYYSQSQGDSEYYDYGHGEVQ DSYEAYGQDDWNGTRPSLKAPPARPVKGAYREHPYGRY

SEQID No:15

ISALQKGYSKVLCQTLSERNSEITSLKNEGENLKRDNAITSGMVSSLQKDILAKDEQVQQ LKEEVSHLKSQNKDKDHQLEALGSRCSVLKEELKQEDAHRELREAQEKELKLCKTVEE KLQEDSRRKLLQLQEMGNRESVIKINLERAVGQLEHFRSQVIKATYGRAKPFRDKPVTD QQLIEKITQVTEDNINFQQKKWTLQKETQLSNSKQEETTENIEKLRTSLDSCQACMKISC CSHDLKKEVDLLQHLQVSPPVSGLQKVVLDVLRHALSWLEEVEQLLRDLGILPSSPNKG FSLYLIYLLEHYKKLMSQAQELQ

SEQID No:16

MVKVTFNSALAQKEAKKDEPKSGEEALIIPPDAVAVDCKDPDDVVPVGQRRAWCWCM CFGLAFMLAGVILGGAYLYKYFALQPDDVYYCGIKYIKDDVILNEPSADAPAALYQTIEEN IKIFEEEEVEFISVPVPEFADSDPANIVHDFNKKLTAYLDLNLDKCYVIPLNTSIVMPPRNL LELLINIKAGTYLPQSYLIHEHMVITDRIENIDHLGFFIYRLCHDKETYKLQRRETIKGIQKR EASNCFAIRHFENKFAVETLICS

SEQID No:17

MASRPRPRTPSRGPSDLRFRGEAGLRRVFLKKAGVRVRPADKRAAGSRVGCPWHRA EPPLGTREQQGFRKRRERWTGGRPGFAQAPPLGGPAQGALRQFPCDVAVGFTQEEW QHLDSAQRTPYRDMMLENYSLLLSVGYCITKPEVVCKLEHGQVLWILEEESPSQSHLDC CIDDDLMEKRQENQDQHLQKVDFVNNKTLTMDRNGVLGKTFSLDTNPILSRKIRGNCD SSGMNLNNISELIISNRSSFVRNPAECNVRGKFLLCMKRENPYARGKPLEYDGNGKAVS QNEDLFRHQYIQTLKQCFEYNQCGKAFHEEAACSTHKRVCSWETL

SEQID No:18

DVIVDINGNCVLGHTHADVVQMFQLVPVNQYVNLTLCRGYPLPDDSEDPVVDIVAATPVI NGQSLTKGETCMNPQDFKPGAMVLEQNGKSGHTLTGDGLNGPSDASEQRVSMASSG

SSQPELVTIPLIKGPKGFGFAIADSPTGQKVKMILDSQWCQGLQKGDIIKEIYHQNVQNLT HLQVVEVLKQFPVGADVPLLILRGGPPSPTKTAKMKTDKKENAGSLEAINEPIPQPMPFP PSIIRSGSPKLDPSEVYLKSKTLYEDKPPNTKDLDVFLRKQESGFGFRVLGGDGPDQSIY IGAIIPLGAAEKDGRLRAADELMCIDGIPVKGKSHKQVLDLMTTAARNGHVLLTVRRKIFY GEKQPEDDSSQAFISTQNGSPRLNRAEVPARPAPQEPYDVVLQRKENEGFGFVILTSK NKPPPGVIPHKIGRVIEGSPADRCGKLKVGDHISAVNGQSIVELSHDNIVQLIKDAGVTVT LTVIAEEEHHGPPSGTNSARQSPALQHRPMGQSQANHIPGDRSALEGEIGKDVSTSYR HSWSDHKHLAQPDTAVISVVGSRHNQNLGCYPVELERGPRGFGFSLRGGKEYNMGLF ILRLAEDGPAIKDGRIHVGDQIVEINGEPTQGITHTRAIELIQAGGNKVLLLLRPGTGLIPD HGDWDINNPSSSNVIYDEQSPLPPSSHFASIFEESHVPVIEESLRVQICEKAEELKDIVPE KKSTLNENQPEIKHQSLLQKNVSKRDPPSSHGHSNKKNLLKVENGVTRRGRSVSPKKP ASQHSEEHLDKIPSPLKNNPKRRPRDQSLSPSKGENKSCQVSTRAGSGQDQCRKSRG RSASPKKQQKIEGSKAPSNAEAKLLEGKSRRIAGYTGSNAEQIPDGKEKSDVIRKDAKQ NQLEKSRTRSPEKKIKRMVEKSLPSKMTNKTTSKEVSENEKGKKVTTGETSSSNDKIGE NVQLSEKRLKQEPEEKVVSNKTEDHKGKELEAADKNKETGRFKPESSSPVKKTLITPGP **WKVPSGNKVTGTIGMAEKRQ**

SEQID No:19

HPPPSALSTPPSPGEGGEFRKRRPRGTQQGHHLQRNMAGAGGGNDIQWCFSQVKGA VDDDVAEADIISTVEFNHSGELLATGDKGGRVVIFQQEQENKIQSHSRGEYNVYSTFQS HEPEFDYLKSLEIEEKINKIRWLPQKNAAQFLLSTNDKTIKLWKISERDKRPEGYNLKEED GRYRDPTTVTTLRVPVFRPMDLMVEASPRRIFANAHTYHINSISINSDYETYLSADDLRIN LWHLEITDRSFNIVDIKPANMEELTEVITAAEFHPNSCNTFVYSSSKGTIRLCDMRASALC DRHSKLFEEPEDPSNRSFFSEIISSISDVKFSHSGRYMMTRDYLSVKIWDLNMENRPVE TYQVHEYLRSKLCSLYENDCIFDKFECCWNGSDSVVMTGSYNNFFRMFDRNTKRDITL EASRENNKPRTVLKPRKVCASGKRKKDEISVDSLDFNKKILHTAWHPKENIIAVATTNNL YIFQDKVN

SEQID No:20

MEKIRVCVRKRPLGMREVRRGEINIITVEDKETLLVHEKKEAVDLTQYILQHVFYFDEVF GEACTNQDVYMKTTHPLIQHIFNGGNATCFAYGQTGAGKTYTMIGTHENPGLYALAAK DIFRQLEVSQPRKHLFVWISFYEIYCGQLYDLLNRRKRY

SEQID No:21

MATSEQSICQARASVMVYDDTSKKWVPIKPGQQGFSRINIYHNTASNTFRVVGVKLQD

-QQVVINYSIVKGLKYNQATPTEHQWRDARQVYGLNFASKEEATTFSNAMLFALNIMNSQ
EGGPSSQRQVQNGPSPDEMDIQRRQVMEQHQQQRQESLERRTSATGPILPPGHPSS
AASAPVSCSGPPPPPPPPPPPPTGATPPPPPPLPAGGAQGSSHDESSMSGLAAAIAG
AKLRRVQRPEDASGGSSPSGTSKSDANRASSGGGGGGLMEEMNKLLAKRRKAASQS
DKPAEKKEDESQMEDPSTSPSPGTRAASQPPNSSEAGRKPWERSNSVEKPVSSILSRT
_PSVAKSPEAKSPLQSQPHSRMKPAGSVNDMALDAFDLDRMKQEILEEVVRELHKVKEE
IIDAIRQELSGISTT

SEQID No:22

MDFQHRPGGKTGSGGVASSSESNRDRRERLRQLALETIDINKDPYFMKNHLGSYECKL CLTLHNNEGSYLAHTQGKKHQTNLARRAAKEAKEAPAQPAPEKVKVEVKKFVKIGRPG YKVTKQRDSEMGQQSLLFQIDYPEIAEGIMPRHRFMSAYEQRIEPPDRRWQYLLMAAE PYETIAFKVPSREIDKAEGKFWTHWNRETKQFFLQFHFKMEKPPAPPSLPAGPPGVKR PPPPLMNGLPPRPPLPESLPPPPPGGLPLPPMPPTGPAPSGPPGPPQLPPPAPGVHPP APVVHPPASGVHPPAPGNHPQ APGVHPQAPGVHPSAPGVHPQAPGVHPSAPGVHPPAPGNHPPPPDTN

SEQID No:23

MAWALKLPLADEVIESGLVQDFDASLSGIGQELGAGAYSMSDVLALPIFKQEESSLPPD
NENKILPFQYVLCAATSPAVKLHDETLTYLNQGQSYEIRMLDNRKLGELPEINGKLVKSIF
RVVFHDRRLQYTEHQQLEGWRWNRPGDRILDIDIPMSVGIIDPRANPTQLNTVEFLWDP
AKRTSVFIQVHCISTEFTMRKHGGEKGVPFRVQIDTFKENENGEYTEHLHSASCQIKVFK
PKGADRKQKTDREKMEKRTPHEKEKYQPSYETTILTECSPWPEITYVNNSPSPGFNSS
HSSFSLGEGNGSPNHQPEPPPPVTDNLLPTTTPQEAQQWLHRNRFSTFTRLFTNFSGA
DLLKLTRDDVIQICGPADGIRLFNALKGRMVRPRLTIYVCQESLQLREQQQQQQQQK
HEDGDSNGTFFVYHAIYLEELTAVELTEKIAQLFSISPCQISQIYKQGPTGIHVLISDEMIQ
NFQEEACFILDTMKAETNDSYHIILK

SEQID No:24

VWRKHYVDGEFASSSVSTGATPPPTRPAALPFLFCRVMAASKTQGAVARMQEDRDGS

CSTVGGVGYGDSKDCILEPLSLPESPGGTTTLEGSPSVPCIFCEEHFPVAEQDKLLKHMI IEHKIVIADVKLVADFQRYILYWRKRFTEQPITDFCSVIRINSTAPFEEQENYFLLCDVLPE DRILREELQKQRLREILEQQQQERNDTNFHGVCMFCNEEFLGNRSVILNHMAREHAFNI GLPDNIVNCNEFLCTLQKKLDNLQCLYCEKTFRDKNTLKDHMRKKQHRKINPKNREYDR FYVINYLELGKSWEEVQLEDDRELLDHQEDDWSDWEEHPASAVCLFCEKQAETIEKLY VHMEDAHEFDLLKIKSELGLNFYQQVKLVNFIRRQVHQCRCYGCHVKFKSKADLRTHM EETKHTSLLPDRKTWDQLEYYFPTYENDTLLCTLSDSESDLTAQEQNENVPIISEDTSKL YALKQSSILNQLLL

SEQID No:25

MRLTHICCCCLLYQLGFLSNGIVSELQFAPDREEWEVVFPALWRREPVDPAGGSGSA DPGWVRGVGGGGSARAQAAGSSREVRSVAPVPLEEPVEGRSESRLRPPPPSEGEED EELESQELPRGSSGAAALSPGAPASWQPPPPPQPPPSPPPAQHAEPDGDEVLLRIPAF SRDLYLLLRRDGRFLAPRFAVEQRPNPGPGPTGAASAPQPPAPPDAGCFYTGAVLRHP GSLASFSTCGGGLMGFIQLNEDFIFIEPLNDTMAITGHPHRVYRQKRSMEEKVTEKSAL HSHYCGIISDKGRPRSRKIAESGRGKRYSYKLPQEYNIETVVVADPAMVSYHGADAARR FILTILNMVFNLFQHKSLGVQVNLRVIKLILLHETPPELYIGHHGEKMLESFCKWQHEEFG KKNDIHLEMSTNWGEDMTSVDAAILITRKDFCVHKDEPCDTVGIAYLSGMCSEKRKCIIA EDNGLNLAFTIAHEMGHNMGINHDNDHPSCADGLHIMSGEWIKGQNLGDVSWSRCSK EDLERFLRSKASNCLLQTNPQSVNSVMVPSKLPGMTYTADEQCQILFGPLASFCQEMQ HVICTGLWCKVEGEKECRTKLDPPMDGTDCDLGKWCKAGECTSRTSAPEHLAGEWSL WSPCSRTCSAGISSRERKCPGLDSEARDCNGPRKQYRICENPPCPAGLPGFRDWQCQ AYSVRTSSPKHILQWQAVLDEEKPCALFCSPVGKEQPILLSEKVMDGTSCGYQGLDICA NGRCQKVGCDGLLGSLAREDHCGVCNGNGKSCKIIKGDFNHTRGAGYVEVLVIPAGAR RIKVVEEKPAHSYLALRDAGKQSINSDWKIEHSGAFNLAGTTVHYVRRGLWEKISAKGP TTAPLHLLVLLFQDQNYGLHYEYTIPSDPLPENQSSKAPEPLFMWTHTSWEDCDATCG GGERKTTVSCTKIMSKNISIVDNEKCKYLTKPEPQIRKCNEQPCQTRWMMTEWTPCSR TCGKGMQSRQVACTQQLSNGTLIRARERDCIGPKPASAQRCEGQDCMTVWEAGVWS **EFSVKCGKGIRHRTVRCTNPRKKCVLSTRPREAEDCEDYSKCYVWRMGDWSKCSITC** GKGMQSRVIQCMHKITGRHGNECFSSEKPAAYRPCHLQPCNEKINVNTITSPRLAALTF KCLGDQWPVYCRVIREKNLCQDMRWYQRCCETCRDFYAQKLQQKS

SEQID No:26

MMKLYIDNAAPDKLKGLCIFFVRCRNDVAINVKTIQEEALFTVLDASKGLLNGIRDMLANI

FLPAVLATNNWGALNQSKQGESEKHIFTETINRYLSFLDGARISIEGTVKLKTIDNVNFSK LHTFEEVTAAASNSETVHQLEEVLMVWYKQIEQVLIESEQMRKEAGDSGPLTELEHWK ** RMSAKFNYIIEQIKGPSCKAVINVLNVAHSKLLKNWRDLDARITDTANESKDNVRYLYTLE KVCQPLYNHDLVSMAHGIQNLINAIRMIHGVSRYYNTSERMTSLFIKVTNQMVTACKAYI TDGGLNHVWDQETPVVLKKIQDCIFLFKEYQASFHKTRKLISESSGEKSFEVSEMYIFGK FEAFCKRLEKITEMITVVQTYSTLSNSTIEGIDIMAIKFRNIYQGVKKKQYDILDPRRTEFD TDFLDFMTKINGLEVQIQAFMNSSFGKILSSQQALQLLQRFQKLNIPCLGLEINHTIERILQ YYVAELDATKKASLYHSQKDDPPLARNMPPIAGKILWVRQLYRRISEPINYFFKNSDILSS PDGKAVIRQYNKISYVLVEFEVVYHTAWIREISQLHYALQATLFVRHPETGKLLVNFDPKI LEVVRETKCMIKMKLDVPEQAKRLLKLESKLKADKLYLQGLLQYYDELCQEVPSVFVNL MTPKMKKVESVLRQGLTVLTWSSLTLESFFQEVELVLDMFNQLLKKISDLCEMHIDTVLK EIAKTVLISLPESGATKVEDMLTLNETYTKEWADILNHKSKHVEEAVRELISIFEQIYEVKY TGKVGKQSEQRKHVVFGSETGEGENNDYEANIVNEFDTHDKEDEFKKECKEVFAFFSH QLLDSLQKATRLSLDTMKRRIFVARQVENMLIILYGRKQSEDIISFIKSEVHLAIPNVVMIP SLDDIQQAINRMIQLTLEVSRGVAHWGQQQIRPIKSVIPSPTTTDVTHQNTGKLLKKEER SFEEAIPARKLKNFYPGVAEHKDISKLVLLLSSSVNSLRKAAHEALQDFQKYKTLWTEDR DVKVKEFLANNPSLTEIRSEILHYATFEQEIDELKPIIVVGALELHTEPMKLALSIEAKAWK MLLCRYLNEEYKKKMSYMIAFINEYLKKLSRPIRDLDDVRFAMEALSCIRDNEIQMDMTL **GPIEEAYAILNRFEVEVTKEESEAVDTLRYSFNKLQSKAVSVQEDLVQVQPKFKSNLLES** VEVFREDVINFAEAYELEGPMVPNIPPQEASNRLQIFQASFDDLWRKFVTYSSGEQLFG LPVTDYEVLHKTRKELNLLQKLYGLYDTVMSSISGYYEILWGDVDIEKINAELLEFQNRC RKLPKGLKDWQAFLDLKKRIDDFSESCPLLEMMTNKAMKQRHWDRISELTGTPFDVES DSFCLRNIMEAPLLKHKDDIEDICISAIKEKDIEAKLTQVIENWTNQNLSFAAFKGKGELLL KGTESGEIITLMEDSLMVLGSLLSNRYNAPFKKNIQNWVYKLSTSSDIIEEWLVVQNLWV YLEAVFVGGDIAKQLPQEAKRFQNIDKSWIKIMQRAHENPNVINCCVGDETMGQLLPHL HEQLEVCQKSLTGYLEKKRLLFPRFFFVSDPVLLEILGQASDSHTIQPHLPAVSDNINEVT FHAKDYDRIMAVISREGEKIVLDNSVMAKGPVEIWLLDLLKMQMSSLHNIIRSAFYQISDS GFQLLPFLSHFPAQVGLLGIQMLWTHDSEEALRNAKDDRKIMQVTNQKFLDILNTLISQT THDLSKFDRVKFETLITIHVHQRDIFDDLVKMHIKSPTDFEWLKQSRFYFKEDLDQTVVSI TDVDFIYQNEFLGCTDRLVITPLTDRCYITLAQALGMNMGGAPAGPAGTGKTETTKDMG RCLGKYVVVFNCSDQMDFRGLGRIFKGKCLAQSGSWGCFDEFNRIELPVLSVAAQQIYI VLTARKERKKQFIFSDGDCVDLNPEFGIFLTMNPGYAGRQELPENLKIQFRTVAMMVPD RQIIMRVKLASCGFLENVILAQKFYVLYKLCEEQLTKQVHYDFGLRNILSVLRTLGSQKRA RPEDSELSIVMRGLRDMNLSKLVDEDEPLFLSLINDLFPGLQLDSNTYAELQNAVAHQV

QIEGLINHPPWNLKLVQLYETSLVRHGLMTLGPSGSGKTTVITILMKAQTECGRPHREM RMNPKAITAPQMFGRLDTATNDWTDGIFSTLWRKTLKAKKGENIFLILDGPVDAIWIENL NSVLDDNKTLTLANGDRIPMAPSCKLLFEVHNIENASPATVSRMGMVYISSSALSWRPIL QAWLKKRTAQEAAVFLTLYEKVFEDTYTYMKLNLNPKMQLLECNYIVQSLNLLEGLIPSK **EEGGVSCVEHLHKLFVFGLMWSLGALLELESREKLEAFLRQHESKLDLPEIPKGSNQTM** YEFYVTDYGDWEHWNKKLQPYYYPTDSIPEYSSILVPNVDNIRTNFLIDTIAKQHKAVLLT GEQGTAKTVMVKAYLKKYDPEVQLSKSLNFSSATEPMMFQRTIESYVDKRIGSTYGPP GGRKMTVFIDDINMPVINEWGDQITNEIVRQMMEMEGMYSLDKPGDFTTIVDVQLIAAMI HPGGGRNDIPQRLKRQFTVFNCTLPSNASIDKIFGIIGCGYFDPCRSFKPQICEMIVNLVS VGRVLWQWTKVKMLPTPSKFHYIFNLRDLSRIWQGMLTIKAEECASIPTLLSLFKHECSR VIADRFITPEDEQWFNAHLTRAVEENIGSDAASCILPEPYFVDFLREMPEPTGDEPEDSV FEVPKIYELMPSFDFLAEKLQFYQRQFNEIIRGTSLDLVFFKDAMTHLIKISRIIRTSCGNA LLVGVGGSGKQSLSRLASFIAGYQIFQITLTRSYNVTNLTDDLKALYKVAGADGKGITFIF TDSEIKDEAFLEYLNNLLSSGEISNLFARDEMDEITQGLISVMKRELPRHPPTFDNLYEYF ISRSRKNLHVVLCFSPVGEKFRARSLKFPGLISGCTMDWFSRWPREALIAVASYFLSDY NIVCSSEIKRQVVETMGLFHDMVSESCESYFQRYRRRAHVTPKSYLSFINGYKNIYAEK VKFINEQAERMNIGLDKLMEASESVAKLSQDLAVKEKELAVASIKADEVLAEVTVSAQAS AKIKNEVQEVKDKAQKIVDEIDSEKVKAESKLEAAKPALEEAEAALNTIKPNDIATVRKLA KPPHLIMRIMDCVLLLFQKKIDPVTMDPEKSCCKPSWGESLKLMSATGFLWSLQQFPKD TINEETVELLQPYFNMDDYTFESAKKVCGNVAGLLSWTLAMAIFYGINREVLPLKANLAK QEGRLAVANAELGKAQALLDEKQAELDKVQAKFDAAMNEKMDLLNDADTCRKKMQAA STLIDGLSGEKIRWTQQSKEFKAQINRLVGDILLCTGFLSYLGPFNQIFRNYLLKDQWEM ELRARKIPFTENLNLISMLVDPPTIGEWGLQGLPGDDLSIQNGIIVTKATRYPLLIDPQTQG KTWIKSKEKENDLQVTSLNHKYFRTHLEDSLSLGRPLLIEDIHEELDPALDNVLEKNFIKS GTTFKVKVGDKECDIMDTFKLYITTKLPNPAFTPEINAKTSVIDFTVTMKGLENQLLRRVIL TEKQELEAERVKLLEDVTFNKRKMKELEDNLLYKLSATKGSLVDDESLIGVLRTTKQTAA EVSEKLHVAAETEIKINAAQEEFRPAATRGSILYFLITEMSMVNIMYQTSLAQFLKLFDQS MARSEKSPLPQKRITNIIEYLTYEVFTYSVRGLYENHKFLFVLLMTLKIDLQRGTVKHREF QALIKGGAALDLKACPPKPYRWILDMTWLNLVELSKLPQFAEIMNQISRNEKGWKSWFD KDAPEEEIIPDGYNDSLDTCHKLLLIRSWCPDRTVFQARKYIADSLEEKYTEPVILNLEKT WEESDTRTPLICFLSMGSDPTNQIDALAKKLKLECRTISMGQGQEVHARKLIQMSMQQ GGWVLLQNCHLGLEFMEELLETLITTEASDDSFRVWITTEPHDRFPITLLQTSLKFTNEP PQGVRAGLKRTFAGINQDLLDISNLPMWKPMLYTVAFLHSTVQERRKFGPLGWNIPYEF NSADFSASVQFIQNHLDECDIKKGVSWNTVRYMIGEVQYGGRVTDDFDKRLLNCFARV

WFSEKMFEPSFCFYTGYKIPLCKTLDQYFEYIQSLPSLDNPEVFGLHPNADITYQSNTAS AVLETITNIQPKESGGGVGETREAIVYRLSEDMLSKLPPDYIPHEVKSRLIKMGHLNSMNI FLRQEIDRMQRVISILRSSLSDLKLAIEGTIIMSENLRDALDNMYDARIPQLWKRVSWDSS TLGFWFTELLERNAQFSTWIFEGRPNVFWMTGFFNPQGFLTAMRQEVTRAHKGWALD TVTIHNEVLRQTKEEITSPPGEGVYIYGLYMDGAAWDRRNGKLMESTPKVLFTQLPVLHI FAINSTAPKDPKLYVCPIYKKPRRTDLTFITVVYLRTVLSPDHWILRGVALLCDIK

SEQID No:27

YLCFPLLFLNPLLFTPCFHLFCENPSRSPFPSSPAGPVMAENDVDNELLDYEDDEVETA AGGDGAEAPAKKDVKGSYVSIHSSGFRDFLLKPELLRAIVDCGFEHPSEVQHECIPQAIL GMDVLCQAKSGMGKTAVFVLATLQQLEPVTGQVSVLVMCHTRELAFQISKEYERFSKY MPNVKVAVFFGGLSIKKDEEVLKKNCPHIVVGTPGRILALARNKSLNLKHIKHFILDECDK MLEQLDMRRDVQEIFRMTPHEKQVMMFSATLSKEIRPVCRKFMQDPMEIFVDDETKLT LHGLQQYYVKLKDNEKNRKLFDLLDVLEFNQVVIFVKSVQRCIALAQLLVEQNFPAIAIHR GMPQEERLSRYQQFKDFQRRILVATNLFGRGMDIERVNIAFNYDMPEDSDTYLHRVAR AGRFGTKGLAITFVSDENDAKILNDVQDRFEVNISELPDEIDISSYIEQTR

SEQID No:28

MSYAEKPDEITKDEWMEKLNNLHVQRADMNRLIMNYLVTEGFKEAAEKFRMESGIEPS VDLETLDERIKIREMILKGQIQEAIALINSLHPELLDTNRYLYFHLQQQHLIELIRQRETEAA LEFAQTQLAEQGEESRECLTEMERTLALLAFDSPEESPFGDLLHTMQRQKVWSEVNQA VLDYENRESTPKLAKLLKLLLWAQNELDQKKVKYPKMTDLSKGVIEEPK

SEQID No:29

MAMQAAKRANIRLPPEVNRILYIRNLPYKITAEEMYDIFGKYGPIRQIRVGNTPETRGTAY VVYEDIFDAKNACDHLSGFNVCNRYLVVLYYNANRAFQKMDTKKKEEQLKLLKEKYGIN TDPPK

SEQID No:30

MRSPATGVPLPTPPPPLLLLLLLLLPPPLLGDQVGPCRSLGSRGRGSSGACAPMGWLC PSSASNLWLYTSRCRDAGTELTGHLVPHHDGLRVWCPESEAHIPLPPAPEGCPWSCR LLGIGGHLSPQGKLTLPEEHPCLKAPRLRCQSCKLAQAPGLRAGERSPEESLGGRRKR NVNTAPQFQPPSYQATVPENQPAGTPVASLRAIDPDEGEAGRLEYTMDALFDSRSNQF FSLDPVTGAVTTAEELDRETKSTHVFRVTAQDHGMPRRSALATLTILVTDTNDHDPVFE

QQEYKESLRENLEVGYEVLTVRATDGDAPPNANILYRLLEGSGGSPSEVFEIDPRSGVI RTRGPVDREEVESYQLTVEASDQGRDPGPRSTTAAVFLSVEDDNDNAPQFSEKRYVV QVREDVTPGAPVLRVTASDRDKGSNAVVHYSIMSGNARGQFYLDAQTGALDVVSPLDY ETTKEYTLRVRAQDGGRPPLSNVSGLVTVQVLDINDNAPIFVSTPFQATVLESVPLGYLV LHVQAIDADAGDNARLEYRLAGVGHDFPFTINNGTGWISVAAELDREEVDFYSFGVEAR DHGTPALTASASVSVTVLDVNDNNPTFTQPEYTVRLNEDAAVGTSVVTVSAVDRDAHS VITYQITSGNTRNRFSITSQSGGGLVSLALPLDYKLERQYVLAVTASDGTRQDTAQIVVN VTDANTHRPVFQSSHYTVNVNEDRPAGTTVVLISATDEDTGENARITYFMEDSIPQFRID ADTGAVTTQAELDYEDQVSYTLAITARDNGIPQKSDTTYLEILVNDVNDNAPQFLRDSYQ GSVYEDVPPFTSVLQISATDRDSGLNGRVFYTFQGGDDGDGDFIVESTSGIVRTLRRLD RENVAQYVLRAYAVDKGMPPARTPMEVTVTVLDVNDNPPVFEQDEFDVFVEENSPIGL AVARVTATDPDEGTNAQIMYQIVEGNIPEVFQLDIFSGELTALVDLDYEDRPEYVLVIQAT SAPLVSRATVHVRLLDRNDNPPVLGNFEILFNNYVTNRSSSFPGGAIGRVPAHDPDISD SLTYSFERGNELSLVLLNASTGELKLSRALDNNRPLEAIMSVLVSDGVHSVTAQCALRVT IITDEMLTHSITLRLEDMSPERFLSPLLGLFIQAVAATLATPPDHVVVFNVQRDTDAPGGH ILNVSLSVGQPPGPGGGPPFLPSEDLQERLYLNRSLLTAISAQRVLPFDDNICLREPCEN YMRCVSVLRFDSSAPFIASSSVLFRPIHPVGGLRCRCPPGFTGDYCETEVDLCYSRPCG PHGRCRSREGGYTCLCRDGYTGEHCEVSARSGRCTPGVCKNGGTCVNLLVGGFKCD **CPSGDFEKPYCQVTTRSFPAHSFITFRGLRQRFHFTLALSFATKERDGLLLYNGRFNEK** HDFVALEVIQEQVQLTFSAGESTTTVSPFVPGGVSDGQWHTVQLKYYNKPLLGQTGLP QGPSEQKVAVVTVDGCDTGVALRFGSVLGNYSCAAQGTQGGSKKSLDLTGPLLLGGV PDLPESFPVRMRQFVGCMRNLQVDSRHIDMADFIANNGTVPGCPAKKNVCDSNTCHN GGTCVNQWDAFSCECPLGFGGKSCAQEMANPQHFLGSSLVAWHGLSLPISQPWYLSL MFRTRQADGVLLQAITRGRSTITLQLREGHVMLSVEGTGLQASSLRLEPGRANDGDWH HAQLALGASGGPGHAILSFDYGQQRAEGNLGPRLHGLHLSNITVGGIPGPAGGVARGF RGCLQGVRVSDTPEGVNSLDPSHGESINVEQGCSLPDPCDSNPCPANSYCSNDWDSY SCSCDPGYYGDNCTNVCDLNPCEHQSVCTRKPSAPHGYTCECPPNYLGPYCETRIDQ PCPRGWWGHPTCGPCNCDVSKGFDPDCNKTSGECHCKENHYRPPGSPTCLLCDCYP TGSLSRVCDPEDGQCPCKPGVIGRQCDRCDNPFAEVTTNGCEVNYDSCPRAIEAGIW WPRTRFGLPAAAPCPKGSFGTAVRHCDEHRGWLPPNLFNCTSITFSELKGFAERLQRN ESGLDSGRSQQLALLLRNATQHTAGYFGSDVKVAYQLATRLLAHESTQRGFGLSATQD VHFTENLLRVGSALLDTANKRHWELIQQTEGGTAWLLQHYEAYASALAQNMRHTYLSP FTIVTPNIVISVVRLDKGNFAGAKLPRYEALRGEQPPDLETTVILPESVFRETPPVVRPAG PGEAQEPEELARRQRRHPELSQGEAVASVIIYRTLAGLLPHNYDPDKRSLRVPKRPIINT

PVVSISVHDDEELLPRALDKPVTVQFRLLETEERTKPICVFWNHSILVSGTGGWSARGC EVVFRNESHVSCQCNHMTSFAVLMDVSRRENGEILPLKTLTYVALGVTLAALLLTFFLT LLRILRSNQHGIRRNLTAALGLAQLVFLLGINQADLPFACTVIAILLHFLYLCTFSWALLEAL HLYRALTEVRDVNTGPMRFYYMLGWGVPAFITGLAVGLDPEGYGNPDFCWLSIYDTLI WSFAGPVAFAVSMSVFLYILAARASCAAQRQGFEKKGPVSGLQPSFAVLLLLSATWLLA LLSVNSDTLLFHYLFATCNCIQGPFIFLSYVVLSKEVRKALKLACSRKPSPDPALTTKSTL TSSYNCPSPYADGRLYQPYGDSAGSLHSTSRSGKSQPSYIPFLLREESALNPGQGPPG LGDPGSLFLEGQDQQHDPDTDSDSDLSLEDDQSGSYASTHSSDSEEEEEEEEEAAF PGEQGWDSLLGPGAERLPLHSTPKDGGPGPGKAPWPGDFGTTAKESSGNGAPEERL RENGDALSREGSLGPLPGSSAQPHKGILKKKCLPTISEKSSLLRLPLEQCTGSSRGSSA SEGSRGPPPRPPPRQSLQEQLNGVMPIAMSIKAGTVDEDSSGSEFLFFNFLH

SEQID No:31

MLRRPAPALAPAARLLLAGLLCGGGVWAARVNKHKPWLEPTYHGIVTENDNTVLLDPP LIALDKDAPLRFAESFEVTVTKEGEICGFKIHGQNVPFDAVVVDKSTGEGVIRSKEKLDC ELQKDYSFTIQAYDCGKGPDGTNVKKSHKATVHIQVNDVNEYAPVFKEKSYKATVIEGK QYDSILRVEAVDADCSPQFSQICSYEIITPDVPFTVDKDGYIKNTEKLNYGKEHQYKLTVT AYDCGKKRATEDVLVKISIKPTCTPGWQGWNNRIEYEPGTGALAVFPNIHLETCDEPVA SVQATVELETSHIGKGCDRDTYSEKSLHRLCGAAAGTAELLPSPSGSLNWTMGLPTDN GHDSDQVFEFNGTQAVRIPDGVVSVSPKEPFTISVWMRHGPFGRKKETILCSSDKTDM NRHHYSLYVHGCRLIFLFRQDPSEEKKYRPAEFHWKLNQVCDEEWHHYVLNVEFPSVT LYVDGTSHEPFSVTEDYPLHPSKIETQLVVGACWQEFSGVENDNETEPVTVASAGGDL HMTQFFRGNLAGLTLRSGKLADKKVIDCLYTCKEGLDLQVLEDSGRGVQIQAHPSQLVL TLEGEDLGELDKAMQHISYLNSRQFPTPGIRRLKITSTIKCFNEATCISVPPVDGYVMVLQ PEEPKISLSGVHHFARAASEFESSEGVFLFPELRIISTITREVEPEGDGAEDPTVQESLVS EEIVHDLDTCEVTVEGEELNHEQESLEVDMARLQQKGIEVSSSELGMTFTGVDTMASY EEVLHLLRYRNWHARSLLDRKFKLICSELNGRYISNEFKVEVNVIHTANPMEHANHMAA QPQFVHPEHRSFVDLSGHNLANPHPFAVVPSTATVVIVVCVSFLVFMIILGVFRIRAAHR RTMRDQDTGKENEMDWDDSALTITVNPMETYEDQHSSEEEEEEEEEEEDGEEEDD ITSAESESSEEEEGEQGDPQNATRQQQLEWDDSTLSY

SEQID No:32

MLPGRLCWVPLLLALGVGSGSGGGGDSRQRRLLAAKVNKHKPWIETSYHGVITENNDT VILDPPLVALDKDAPVPFAGEICAFKIHGQELPFEAVVLNKTSGEGRLRAKSPIDCELQKE YTFIIQAYDCGAGPHETAWKKSHKAVVHIQVKDVNEFAPTFKEPAYKAVVTEGKIYDSIL QVEAIDEDCSPQYSQICNYEIVTTDVPFAIDRNGNIRNTEKLSYDKQHQYEILVTAYDCG QKPAAQDTLVQVDVKPVCKPGWQDWTKRIEYQPGSGSMPLFPSIHLETCDGAVSSLQI VTELQTNYIGKGCDRETYSEKSLQKLCGASSGIIDLLPSPSAATNWTAGLLVDSSEMIFK FDGRQGAKIPDGIVPKNLTDQFTITMWMKHGPSPGVRAEKETILCNSDKTEMNRHHYAL YVHNCRLVFLLRKDFDQADTFRPAEFHWKLDQICDKEWHYYVINVEFPVVTLYMDGAT YEPYLVTNDWPIHPSHIAMQLTVGACWQGGEVTKPQFAQFFHGSLASLTIRPGKMESQ KVISCLQACKEGLDINSLESLGQGIKYHFNPSQSILVMEGDDIGNINRALQKVSYINSRQF PTAGVRRLKVSSKVQCFGEDVCISIPEVDAYVMVLQAIEPRITLRGTDHFWRPAAQFES ARGVTLFPDIKIVSTFAKTEAPGDVKTTDPKSEVLEEMLHNLDFCDILVIGGDLDPRQECL ELNHSELHQRHLDATNSTAGYSIYGVGSMSRYEQVLHHIRYRNWRPASLEARRFRIKC SELNGRYTSNEFNLEVSILHEDQVSDKEHVNHLIVQPPFLQSVHHPESRSSIQHSSVVP SIATVVIIISVCMLVFVVAMGVYRVRIAHQHFIQETEAAKESEMDWDDSALTITVNPMEKH EGPGHGEDETEGEEEEEAEEMSSSSGSDDSEEEEEEEGMGRGRHGQNGARQAQL EWDDSTLPY

SEQID No:33

MTLLLLPLLLASLLASCSCNKANKHKPWIEAEYQGIVMENDNTVLLNPPLFALDKDAPLR YAGEICGFRLHGSGVPFEAVILDKATGEGLIRAKEPVDCEAQKEHTFTIQAYDCGEGPD GANTKKSHKATVHVRVNDVNEFAPVFVERLYRAAVTEGKLYDRILRVEAIDGDCSPQYS QICYYEILTPNTPFLIDNDGNIENTEKLQYSGERLYKFTVTAYDCGKKRAADDAEVEIQVK PTCKPSWQGWNKRIEYAPGAGSLALFPGIRLETCDEPLWNIQATIELQTSHVAKGCDRD NYSERALRKLCGAATGEVDLLPMPGPNANWTAGLSVHYSQDSSLIYWFNGTQAVQVP LGGPSGLGSGPQDSLSDHFTLSFWMKHGVTPNKGKKEEETIVCNTVQNEDGFSHYSLT VHGCRIAFLYWPLLESARPVKFLWKLEQVCDDEWHHYALNLEFPTVTLYTDGISFDPALI HDNGLIHPPRREPALMIGACWTEEKNKEKEKGDNSTDTTQGDPLSIHHYFHGYLAGFS VRSGRLESREVIECLYACREGLDYRDFESLGKGMKVHVNPSQSLLTLEGDDVETFNHA LQHVAYMNTLRFATPGVRPLRLTTAVKCFSEESCVSIPEVEGYVVVLQPDAPQILLSGTA HFARPAVDFEGTNGVPLFPDLQITCSISHQVEAKKDESWQGTVTDTRMSDEIVHNLDG CEISLVGDDLDPERESLLLDTTSLQQRGLELTNTSAYLTIAGVESITVYEEILRQARYRLR HGAALYTRKFRLSCSEMNGRYSSNEFIVEVNVLHSMNRVAHPSHVLSSQQFLHRGHQP PPEMAGHSLASSHRNSMIPSAATLIIVVCVGFLVLMVVLGLVRIHSLHRRVSGAGGPPGA SSDPKDPDLFWDDSALTIIVNPMESYQNRQSCVTGAVGGQQEDEDSSDSEVADSPSS DERRIIETPPHRY

SEQID No:34

MYIKQVIIQGERSYRDQTIVDPFSSKHNVIVGRNGSGKSNFFYAIQFVLSDEFSHLRPEQ RLALLHEGTGPRVISAFVEIIFDNSDNRLPIDKEEVSLRRVIGAKKDQYFLDKKMVTKNDV MNLLESAGESRSNPYYIVKQGKINQMATAPDSQRLKLLREVAGTRVYDERKEESISLMK ETEGKREKINELLKYIEERLHTLEEEKEELAQYQKWDKMRRALEYTIYNQELNETRAKLD ELSAKRETSGEKSRQLRDAQQDARDKMEDIERQVRELKTKISAMKEEKEQLSAERQEQ IKQRTKLELKAKDLQDELAGNSEQRKRLLKERQKLLEKIEEKQKELAETEPKFNSVKEKE **ERGIARLAQATQERTDLYAKQGRGSQFTSKEERDKWIKKELKSLDQAINDKKRQIAAIHK** DLEDTEANKEKNLEQYNKLDQDLNEVKARVEELDRKYYEVKNKKDELQSERNYLWREE NAEQQALAAKREDLEKKQQLLRAATGKAILNGIDSINKVLDHFRRKGINQHVQNGYHGIV MNNFECEPAFYTCVEVTAGNRLFYHIVDSDEVSTKILMEFNKMNLPGEVTFLPLNKLDV RDTAYPETNDAIPMISKLRYNPRFDKAFKHVFGKTLICRSMEVSTQLARAFTMDCITLEG DQVSHRGALTGGYYDTRKSRLELQKDVRKAEEELGELEAKLNENLRRNIERINNEIDQL MNQMQQIETQQRKFKASRDSILSEMKMLKEKRQQSEKTFMPKQRSLQSLEASLHAME STRESLKAELGTDLLSQLSLEDQKRVDALNDEIRQLQQENRQLLNERIKLEGIITRVETYL NENLRKRLDQVEQELNELRETEGGTVLTATTSELEAINKRVKDTMARSEDLDNSIDKTE AGIKELQKSMERWKNMEKEHMDAINHDTKELEKMTNRQGMLLKKKEECMKKIRELGSL PQEAFEKYQTLSLKQLFRKLEQCNTELKKYSHVNKKALDQFVNFSEQKEKLIKRQEELD RGYKSIMELMNVLELRKYEAIQLTFKQVSKNFSEVFQKLVPGGKATLVMKKGDVEGSQS QDEGEGSGESERGSGSQSSVPSVDQFTGVGIRVSFTGKQGEMREMQQLSGGQKSLV ALALIFAIQKCDPAPFYLFDEIDQALDAQHRKAVSDMIMELAVHAQFITTTFRPELLESAD KFYGVKFRNKVSHIDVITAEMAKDFVEDDTTHG

SEQID No:35

MAVTLDKDAYYRRVKRLYSNWRKGEDEYANVDAIVVSVGVDEEIVYAKSTALQTWLFG
YELTDTIMVFCDDKIIFMASKKKVEFLKQIANTKGNENANGAPAITLLIREKNESNKSSFD
KMIEAIKESKNGKKIGVFSKDKFPGEFMKSWNDCLNKEGFDKIDISAVVAYTIAVKEDGE
LNLMKKAASITSEVFNKFFKERVMEIVDADEKVRHSKLAESVEKAIEEKKYLAGADPSTV
EMCYPPIIQSGGNYNLKFSVVSDKNHMHFGAITCAMGIRFKSYCSNLVRTLMVDPSQEV
QENYNFLLQLQEELLKELRHGVKICDVYNAVMDVVKKQKPELLNKITKNLGFGMGIEFR
EGSLVINSKNQYKLKKGMVFSINLGFSDLTNKEGKKPEEKTYALFIGDTVLVDEDGPATV
LTSVKKKVKNVGIFLKNEDEEEEEEEKDEAEDLLGRGSRAALLTERTRNEMTAEEKRRA
HQKELAAQLNEEAKRRLTEQKGEQQIQKARKSNVSYKNPSLMPKEPHIR

EMKIYIDKKYETVIMPVFGIATPFHIATIKNISMSVEGDYTYLRINFYCPGSALGRNEGNIF PNPEATFVKEITYRASNIKAPGEQTVPALNLQNAFRIIKEVQKRYKTREAEEKEKEGIVKQ DSLVINLNRSNPKLKDLYIRPNIAQKRMQGSLEAHVNGFRFTSVRGDKVDILYNNIKHAL FQPCDGEMIIVLHFHLKNAIMFGKKRHTDVQFYTEVGEITTDLGKHQHMHDRDDLYAEQ MEREMRHKLKTAFKNFIEKVEALTKEELEFEVPFRDLGFNGAPYRSTCLLQPTSSALVN ATEWPPFVVTLDEVELIHFERVQFHLKNFDMVIVYKDYSKKVTMINAIPVASLDPIKEWLN SCDLKYTEGVQSLNWTKIMKTIVDDPEGFFEQGGWSFLEPEGEGSDAEEGDSESEIED ETFNPSEDDYEEEEEDSDEDYSSEAEESDYSKESLGSEEESGKDWDELEEEARKADR ESRYEEEEEQSRSMSRKRKASVHSSGRGSNRGSRHSSAPPKKKRK

SEQID No:36

MVVSKMNKDAQMRAAINQKLIETGERERLKELLRAKLIECGWKDQLKAHCKEVIKEKGL EHVTVDDLVAEITPKGRALVPDSVKKELLQRIRTFLAQHASL

SEQID No:37

MENHKSNNKENITIVDISRKINQLPEAERNLLENGSVYVGLNAALCGLIANSLFRRILNVT KARIAAGLPMAGIPFLTTDLTYRCFVSFPLNTGDLDCETCTITRSGLTGLVIGGLYPVFLAI PVNGGLAARYQSALLPHKGNILSYWIRTSKPVFRKMLFPILLQTMFSAYLGSEQYKLLIK ALQLSEPGKEIH

SEQID No:38

MAEVEETLKRLQSQKGVQGIIVVNTEGIPIKSTMDNPTTTQYASLMHSFILKARSTVRDID PQNDLTFLRIRSKKNEIMVAPDKDYFLIVIQNPTE

SEQID No:39

MAAVGRVGSFGSSPPGLSSTYTGGPLGNEIASGNGGAAAGDDEDGQNLWSCILSEVS TRSRSKLPAGKNVLLLGEDGAGKTSLIRKIQGIEEYKKGRGLEYLYLNVHDEDRDDQTR CNVWILDGDLYHKGLLKFSLDAVSLKDTLVMLVVDMSKPWTALDSLQKWASVVREHVD KLKIPPEEMKQMEQKLIRDFQEYVEPGEDFPASPQRRNTASQEDKDDSVVVPLGADTL THNLGIPVLVVCTKCDAISVLEKEHDYRDEHFDFFQSHIRKFCLRYGAALIYTSVKENKNI DLVYKYIVQKLYGFPYKIPAVVVEKDAVFIPAGWDNDKKIGILHENFQTLKAEDNFEDIITK PPVRKFVHEKEIMAEDDQVFLMKLQSLLAKQPPTAAGRPVDASPRVPGGSPRTPNRSV SSNVASVSPIPAGSKKIDPNMKAGATSEGVLANFFNSLLSKKTGSPGGPGVSGGSPAG GAGGGSSGLPPSTKKSGQKPVLDVHAELDRITRKPVTVSPTTPTSPTEGEAS

SEQID No:40

MVTQILGAMESQVGGGPAGPALPNGPLLGTNGATDDSKTNLIVNYLPQNMTQDEFKSL FGSIGDIESCKLVRDKITGQSLGYGFVNYSDPNDADKAINTLNGLKLQTKTIKVSYARPSS ASIRDANLYVSGLPKTMSQKEMEQLFSQYGRIITSRILVDQVTGVSRGVGFIRFDKRIEA EEAIKGLNGQKPLGAAEPITVKFANNPSQKTGQALLTHLYQSSARRYAGPLHHQTQRFR LDNLLNMAYGVKSPLSLIARFSPIAIDGMSGLAGVGLSGGAAGAGWCIFVYNLSPEADE SVLWQLFGPEGAVTNVKVIRDETTNKCKGEGEVTMTNYDEAAMAIASLNGYRLGERVL QVSFKTSKQHKA

SEQID No:41

MVCTCVEGDNQFIVTEIPHVRQLISGDGVGECAVRAATEGRTLILEGLEKAERNVLPVLN NLLENREMQLEDGRFLMSAERYDKLLRDHTKKELDSWKIVRVSENFRVIALGLPVPRYS GNPLDPPLRSRFQARDIYYLPFKDQLKLLYSIGANVSAEKVSQLLSFATTLCSQESSTLG LPDFPLDSLAAAVQILDSFPMMPIKHAIQWLYPYSILLGHEGKMAVEGVLKRFELQDSGS SLLPKEIVKVEKMMENHVSQASVTIRIADKEVTIK

SEQID No:42

MSASQDSRSRDNGPDGMEPEGVIESNWNEIVDSFDDMNLSESLLRGIYAYGFEKPSAI QQRAILPCIKGYDVIAQAQSGTGKTATFAISILQQIELDLKATQALVLAPTRELAQQIQKVV MALGDYMGASCHACIGGTNVRAEVQKLQMEAPHIIVGTPGRVFDMLNRRYLSPKYIKM FVLDEADEMLSRGFKDQIYDIFQKLNSNTQVVLLSATMPSDVLEVTKKFMRDPIRILVKK EELTLEGIRQFYINVEREEWKLDTLCDLYETLTITQAVIFINTRRKVDWLTEKMHARDFTV SAMHGDMDQKERDVIMREFRSGSSRVLITTDLLARGIDVQQVSLVINYDLPTNRENYIH RIGRGGRFGRKGVAINMVTEEDKRTLRDIETFYNTSIEEMPLNVADLI

SEQID No:43

MDQCVTVERELEKVLHKFSGYGQLCERGLEELIDYTGGLKHEILQSHGQDAELSGTLSL VLTQCCKRIKDTVQKLASDHKDIHSSVSRVGKAIDKNFDSDISSVGIDGCWQADSQRLL NEVMVEHFFRQGMLDVAEELCQESGLSVDPSQKEPFVELNRILEALKVRVLRPALEWA VSNREMLIAQNSSLEFKLHRLYFISLLMGGTTNQREALQYAKNFQPFALNHQKDIQVLM GSLVYLRQGIENSPYVHLLDANQWADICDIFTRDACALLGLSVESPLSVSFSAGCVALPA LINIKAVIEQRQCTGVWNQKDELPIEVDLGKKCWYHSIFACPILRQQTTDNNPPMKLVCG HIISRDALNKMFNGSKLKCPYCPMEQSPGDAKQIFF

SEQID No:44

MLGTGPAAATTAATTSSNVSVLQQFASGLKSRNEETRAKAAKELQHYVTMELREMSQE **ESTRFYDQLNHHIFELVSSSDANERKGGILAIASLIGVEGGNATRIGRFANYLRNLLPSND** PVVMEMASKAIGRLAMAGDTFTAEYVEFEVKRALEWLGADRNEGRRHAAVLVLRELAI SVPTFFFQQVQPFFDNIFVAVWDPKQAIREGAVAALRACLILTTQREPKEMQKPQWYR HTFEEAEKGFDETLAKEKGMNRDDRIHGALLILNELVRISSMEGERLREEMEEITQQQLV HDKYCKDLMGFGTKPRHITPFTSFQAVQPQQSNALVGLLGYSSHQGLMGFGTSPSPAK STLVESRCCRDLMEEKFDQVCQWVLKCRNSKNSLIQMTILNLLPRLAAFRPSAFTDTQY LQDTMNHVLSCVKKEKERTAAFQALGLLSVAVRSEFKVYLPRVLDIIRAALPPKDFAHKR QKAMQVDATVFTCISMLARAMGPGIQQDIKELLEPMLAVGLSPALTAVLYDLSRQIPQLK KDIQDGLLKMLSLVLMHKPLRHPGMPKGLAHQLASPGLTTLPEASDVGSITLALRTLGSF **EFEGHSLTQFVRHCADHFLNSEHKEIRMEAARTCSRLLTPSIHLISGHAHVVSQTAVQV** VADVLSKLLVVGITDPDPDIRYCVLASLDERFDAHLAQAENLQALFVALNDQVFEIRELAI CTVGRLSSMNPAFVMPFLRKMLIQILTELEHSGIGRIKEQSARMLGHLVSNAPRLIRPYM **EPILKALILKLKDPDPDPNPGVINNVLATIGELAQVSGLEMRKWVDELFIIIMDMLQDSSLL** AKRQVALWTLGQLVASTGYVVEPYRKYPTLLEVLLNFLKTEQNQGTRREAIRVLGLLGA LDPYKHKVNIGMIDQSRDASAVSLSESKSSQDSSDYSTSEMLVNMGNLPLDEFYPAVS MVALMRIFRDQSLSHHHTMVVQAITFIFKSLGLKCVQFLPQVMPTFLNVIRVCDGAIREF LFQQLGMLVSFVKSHIRPYMDEIVTLMREFWVMNTSIQSTIILLIEQIVVALGGEFKLYLPQ LIPHMLRVFMHDNSPGRIVSIKLLAAIQLFGANLDDYLHLLLPPIVKLFDAPEAPLPSRKAA LETVDRLTESLDFTDYASRIIHPIVRTLDQSPELRSTAMDTLSSLVFQLGKKYQIFIPMVNK VLVRHRINHQRYDVLICRIVKGYTLADEEEDPLIYQHRMLRSGQGDALASGPVETGPMK KLHVSTINLQKAWGAARRVSKDDWLEWLRRLSLELLKDSSSPSLRSCWALAQAYNPMA RDLFNAAFVSCWSELNEDQQDELIRSIELALTSQDIAEVTQTLLNLAEFMEHSDKGPLPL RDDNGIVLLGERAAKCRAYAKALHYKELEFQKGPTPAILESLISINNKLQQPEAAAGVLE YAMKHFGELEIQATWYEKLHEWEDALVAYDKKMDTNKDDPELMLGRMRCLEALGEWG QLHQQCCEKWTLVNDETQAKMARMAAAAAWGLGQWDSMEEYTCMIPRDTHDGAFY RAVLALHQDLFSLAQQCIDKARDLLDAELTAMAGESYSRAYGAMVSCHMLSELEEVIQY KLVPERREIIRQIWWERLQGCQRIVEDWQKILMVRSLVVSPHEDMRTWLKYASLCGKS GRLALAHKTLVLLLGVDPSRQLDHPLPTVHPQVTYAYMKNMWKSARKIDAFQHMQHFV QTMQQQAQHAIATEDQQHKQELHKLMARCFLKLGEWQLNLQGINESTIPKVLQYYSAA **TEHDRSWYKAWHAWAVMNFEAVLHYKHQNQARDEKKKLRHASGANITNATTAATTAA** TATTTASTEGSNSESEAESTENSPTPSPLQKKVTEDLSKTLLMYTVPAVQGFFRSISLSR

GNNLQDTLRVLTLWFDYGHWPDVNEALVEGVKAIQIDTWLQVIPQLIARIDTPRPLVGRL
IHQLLTDIGRYHPQALIYPLTVASKSTTTARHNAANKILKNMCEHSNTLVQQAMMVSEELI
RVAILWHEMWHEGLEEASRLYFGERNVKGMFEVLEPLHAMMERGPQTLKETSFNQAY
GRDLMEAQEWCRKYMKSGNVKDLTQAWDLYYHVFRRISKQLPQLTSLELQYVSPKLL
MCRDLELAVPGTYDPNQPIIRIQSIAPSLQVITSKQRPRKLTLMGSNGHEFVFLLKGHED
LRQDERVMQLFGLVNTLLANDPTSLRKNLSIQRYAVIPLSTNSGLIGWVPHCDTLHALIR
DYREKKKILLNIEHRIMLRMAPDYDHLTLMQKVEVFEHAVNNTAGDDLAKLLWLKSPSS
EVWFDRRTNYTRSLAVMSMVGYILGLGDRHPSNLMLDRLSGKILHIDFGDCFEVAMTR
EKFPEKIPFRLTRMLTNAMEVTGLDGNYRITCHTVMEVLREHKDSVMAVLEAFVYDPLL
NWRLMDTNTKGNKRSRTRTDSYSAGQSVEILDGVELGEPAHKKTGTTVPESIHSFIGD
GLVKPEALNKKAIQIINRVRDKLTGRDFSHDDTLDVPTQVELLIKQATSHENLCQCYIGW
CPFW

SEQID No:45

MMNNSGYSDAGLGLGDETDEMPSTEKDLAEDAPWKKIQQNTFTRWCNEHLKCVGKRL TDLQRDLSDGLRLIALLEVLSQKRMYRKFHPRPNFRQMKLENVSVALEFLEREHIKLVSI DSKAIVDGNLKLILGLIWTLILHYSISMPMWEDEDDEDARKQTPKQRLLGWIQNKVPQLPI TNFNRDWQDGKALGALVDNCAPGLCPDWEAWDPNQPVENAREAMQQADDWLGVPQ VIAPEEIVDPNVDEHSVMTYLSQFPKAKLKPGAPVRSKQLNPKKAIAYGPGIEPQGNTVL QPAHFTVQTVDAGVGEVLVYIEDPEGHTEEAKVVPNNDKDRTYAVSYVPKVAGLHKVT VLFAGQNIERSPFEVNVGMALGDANKVSARGPGLEPVGNVANKPTYFDIYTAGAGTGD VAVVIVDPQGRRDTVEVALEDKGDSTFRCTYRPAMEGPHTVHVAFAGAPITRSPFPVH VSEACNPNACRASGRGLQPKGVRVKEVADFKVFTKGAGSGELKVTVKGPKGTEEPVK VREAGDGVFECEYYPVVPGKYVVTITWGGYAIPRSPFEVQVSPEAGVQKVRAWGPGL **ETGQVGKSADFVVEAIGTEVGTLGFSIEGPSQAKIECDDKGDGSCDVRYWPTEPGEYA** VHVICDDEDIRDSPFIAHILPAPPDCFPDKVKAFGPGLEPTGCIVDKPAEFTIDARAAGKG DLKLYAQDADGCPIDIKVIPNGDGTFRCSYVPTKPIKHTIIISWGGVNVPKSPFRVNVGEG SHPERVKVYGPGVEKTGLKANEPTYFTVDCSEAGQGDVSIGIKCAPGVVGPAEADIDFD IIKNDNDTFTVKYTPPGAGRYTIMVLFANQEIPASPFHIKVDPSHDASKVKAEGPGLNRT GVEVGKPTHFTVLTKGAGKAKLDVQFAGTAKGEVVRDFEIIDNHDYSYTVKYTAVQQG NMAVTVTYGGDPVPKSPFVVNVAPPLDLSKIKVQGLNSKVAVGQEQAFSVNTRGAGG QGQLDVRMTSPSRRPIPCKLEPGGGAEAQAVRYMPPEEGPYKVDITYDGHPVPGSPF AVEGVLPPDPSKVCAYGPGLKGGLVGTPAPFSIDTKGAGTGGLGLTVEGPCEAKIECQ DNGDGSCAVSYLPTEPGEYTINILFAEAHIPGSPFKATIRPVFDPSKVRASGPGLERGKV

GEAATFTVDCSEAGEAELTIEILSDAGVKAEVLIHNNADGTYHITYSPAFPGTYTITIKYGG HPVPKFPTRVHVQPAVDTSGVKVSGPGVEPHGVLREVTTEFTVDARSLTATGGNHVTA RVÉNPSGAKTDTYVTDNGDGTYRVQYTAYEEGVHLVEVLYDEVAVPKSPFRVGVTEGC DPTRVRAFGPGLEGGLVNKANRFTVETRGAGTGGLGLAIEGPSEAKMSCKDNKDGSC TVEYIPFTPGDYDVNITFGGRPIPGSPFRVPVKDVVDPGKVKCSGPGLGAGVRARVPQT FTVDCSQAGRAPLQVAVLGPTGVAEPVEVRDNGDGTHTVHYTPATDGPYTVAVKYAD QEVPRSPFKIKVLPAHDASKVRASGPGLNASGIPASLPVEFTIDARDAGEGLLTVQILED PEGKPKKANIRDNGDGTYTVSYLPDMSGRYTITIKYGGDEIPYSPFRIHALPTGDASKCL VTVSIGGHGLGACLGPRIQIGQETVITVDAKAAGEGKVTCTVSTPDGAELDVDVVENHD GTFDIYYTAPEPGKYVITIRFGGEHIPNSPFHVLACDPLPHEEEPSEVPQLRQPYAPPRP GARPTHWATEEPVVPVEPMESMLRPFNLVIPFAVQKGELTGEVRMPSGKTARPNITDN KDGTITVRYAPTEKGLHQMGIKYDGNHIPGSPLQFYVDAINSRHVSAYGPGLSHGMVNK PATFTIVTKDAGEGGLSLAVEGPSKAEITCKDNKDGTCTVSYLPTAPGDYSIIVRFDDKHI PGSPFTAKITGDDSMRTSQLNVGTSTDVSLKITESDLSQLTASIRAPSGNEEPCLLKRLP NRHIGISFTPKEVGEHVVSVRKSGKHVTNSPFKILVGPSEIGDASKVRVWGKGLSEGHT FQVAEFIVDTRNAGYGGLGLSIEGPSKVDINCEDMEDGTCKVTYCPTEPGTYIINIKFADK HVPGSPFTVKVTGEGRMKESITRRRQAPSIATIGSTCDLNLKIPGNWFQMVSAQERLTR TFTRSSHTYTRTERTEISKTRGGETKREVRVEESTQVGGDPFPAVFGDFLGRERLGSF GSITRQQEGEASSQDMTAQVTSPSGKVEAAEIVEGEDSAYSVRFVPQEMGPHTVAVKY RGQHVPGSPFQFTVGPLGEGGAHKVRAGGTGLERGVAGVPAEFSIWTREAGAGGLSI AVEGPSKAEIAFEDRKDGSCGVSYVVQEPGDYEVSIKFNDEHIPDSPFVVPVASLSDDA RRLTVTSLQETGLKVNQPASFAVQLNGARGVIDARVHTPSGAVEECYVSELDSDKHTIR FIPHENGVHSIDVKFNGAHIPGSPFKIRVGEQSQAGDPGLVSAYGPGLEGGTTGVSSEFI VNTLNAGSGALSVTIDGPSKVQLDCRECPEGHVVTYTPMAPGNYLIAIKYGGPQHIVGS PFKAKVTGPRLSGGHSLHETSTVLVETVTKSSSSRGSSYSSIPKFSSDASKVVTRGPGL SQAFVGQKNSFTVDCSKAGTNMMMVGVHGPKTPCEEVYVKHMGNRVYNVTYTVKEK **GDYILIVKWGDESVPGSPFKVKVP**

SEQID No:46

RQAWHEVAAPSWRGARLVQSALRVWQVGPHVARERVIPFSSLLGFQRRCVSCVAGS AFSGPRLASASRSNGQGSALDHFLGFSQPDSSVTPCVPAVSMNRDEQDVLLVHHPDM PENSRVLRVVLLGAPNAGKSTLSNQLLGRKVFPVSRKVHTTRCQALGVITEKETQVILLD TPGIISPGKQKRHHLELSLLEDPWKSMESADLVVVLVDVSDKWTRNQLSPQLLRCLTKY SQIPSVLVMNKVDCLKQKSVLLELTAALTEGVVNGKKLKMRQAFHSHPGTHCPSPAVK

DPNTQSVGNPQRIGWPHFKEIFMLSALSQEDVKTLKQYLLTQAQPGPWEYHSAVLTSQ TPEEICANIIREKLLEHLPQEVPYNVQQKTAVWEEGPGGELVIQQKLLVPKESYVKLLIGP KGHVISQIAQEAGHDLMDIFLCDVDIRLSVKLLK

SEQID No:47

MAAACRSVKGLVAVITGGASGLGLATAERLVGQGASAVLLDLPNSGGEAQAKKLGNNC VFAPADVTSEKDVQTALALAKGKFGRVDVAVNCAGIAVASKTYNLKKGQTHTLEDFQRV LDVNLMGTFNVIRLVAGEMGQNEPDQGGQRGVIINTASVAAFEGQVGQAAYSASKGGI VGMTLPIARDLAPIGIRVMTIAPGLFGTPLLTSLPEKVCNFLASQVPFPSRLGDPAEYAHL VQAIIENPFLNGEVIRLDGAIRMQP

SEQID No:48

MAYSQGGKKKVCYYYDGDIGNYYYGQGHPMKPHRIRMTHNLLLNYGLYRKMEIYRP HKATAEEMTKYHSDEYIKFLRSIRPDNMSEYSKQMHIFNVGEDCPAFDGLFEFCQLSTG GSVAGAVKLNRQQTDMAVNWAGGLHHAKKYEASGFCYVNDIVLAILELLKYHQRVLYID IDIHHGDGVEEAFYTTDRVMTVSFHKYGEYFPGTGDLRDIGAGKGKYYAVNFPMCDGID DESYGQIFKPIISKVMEMYQPSAVVLQCGADSLSGDRLGCFNLTVKGHAKCVEVVKTFN LPLLMLGGGGYTIRNVARCWTYETAVALDCEIPNELPYNDYFEYFGPDFKLHISPSNMT NQNTPEYMEKIKQRLFENLRMLPHAPGVQMQAIPEDAVHEDSGDEDGEDPDKRISIRA SDKRIACDEEFSDSEDEGEGGRRNVADHKKGAKKARIEEDKKETEDKKTDVKEEDKSK DNSGEKTDTKGTKSEQLSNP

SEQID No:49

MPSESFCLAAQARLDSKWLKTDIQLAFTRDGLCGLWNEMVKDGEIVYTGTESTQNGEL
PPRKDDSVEPSGTKKEDLNDKEKKDEEETPAPIYRAKSILDSWVWGKQPDVNELKECL
SVLVKEQQALAVQSATTTLSALRLKQRLVILERYFIALNRTVFQENVKVKWKSSGISLPP
VDKKSSRPAGKGVEGLARVGSRAALSFAFAFLRRAWRSGEDADLCSELLQESLDALRA
LPEASLFDESTVSSVWLEVVERATRFLRSVVTGDVHGTPATKGPGSIPLQDQHLALAILL
ELAVQRGTLSQMLSAILLLLQLWDSGAQETDNERSAQGTSAPLLPLLQRFQSIICRKDAP
HSEGDMHLLSGPLSPNESFLRYLTLPQDNELAIDLRQTAVVVMAHLDRLATPCMPPLCS
SPTSHKGSLQEVIGWGLIGWKYYANVIGPIQCEGLANLGVTQIACAEKRFLILSRNGRVY
TQAYNSDTLAPQLVQGLASRNIVKIAAHSDGHHYLALAATGEVYSWGCGDGGRLGHGD
TVPLEEPKVISAFSGKQAGKHVVHIACGSTYSAAITAEGELYTWGRGNYGRLGHGSSED
EAIPMLVAGLKGLKVIDVACGSGDAQTLAVTENGQVWSWGDGDYGKLGRGGSDGCKT

PKLIEKLQDLDVVKVRCGSQFSIALTKDGQVYSWGKGDNQRLGHGTEEHVRYPKLLEG LQGKKVIDVAAGSTHCLALTEDSEVHSWGSNDQCQHFDTLRVTKPEPAALPGLDTKHIV GIACGPAQSFAWSSCSEWSIGLRVPFVVDICSMTFEQLDLLLRQVSEGMDGSADWPPP QEKECVAVATLNLLRLQLHAAISHQVDPEFLGLGLGSILLNSLKQTVVTLASSAGVLSTV QSAAQAVLQSGWSVLLPTAEERARALSALLPCAVSGNEVNISPGRRFMIDLLVGSLMAD GGLESALHAAITAEIQDIEAKKEAQKEKEIDEQEANASTFHRSRTPLDKDLINTGICESSG KQCLPLVQLIQQLLRNIASQTVARLKDVARRISSCLDFEQHSRERSASLDWLLRFQRLLI SKLYPGESIGQTSDISSPELMGVGSLLKKYTALLCTHIGDILPVAASIASTSWRHFAEVAYI VEGDFTGVLLPELVVSIVLLLSKNADLMQEAGAVPLLGGLLEHLDRFNHLAPGKERDDH **EELAWPGIMESFFTGQNCRNNEEVTLIRKADLENHNKDGGFWTVIDGKVYDIKDFQTQS** LTGNSILAQFAGEDPVVALEAALQFEDTRESMHAFCVGQYLEPDQEIVTIPDLGSLSSPLI DTERNLGLLLGLHASYLAMSTPLSPVEIECAKWLQSSIFSGGLQTSQIHYRYNEEKDED HCSSPGGTPASKSRLCSHRRALGDHSQAFLQAIADNNIQDHNVKDFLCQIERYCRQCH LTTPIMFPPEHPVEEVGRLLLCCLLKHEDLGHVALSLVHAGALGIEQVKHRTLPKSVVDV CRVVYQAKCSLIKTHQEQGRSYKEVCAPVIERLRFLFNELRPAVCNDLSIMSKFKLLSSL PRWRRIAQKIIRERRKKRVPKKPESMDDEEKIGNEESDLEEACILPHSPINVDKRPIAIKS PKDKWQPLLSTVTGVHKYKWLKQNVQGLYPQSPLLSTIAEFALKEEPVDVEKMRKCLL KQLERAEVRLEGIDTILKLASKNFLLPSVQYAMFCGWQRLIPEGIDIGEPLTDCLKDVDLI PPFNRMLLEVTFGKLYAWAVQNIRNVLMDASATFKELGIQPVPLQTITNENPSGPSLGTI PQARFLLVMLSMLTLQHGANNLDLLLNSGMLALTQTALRLIGPSCDNVEEDMNASAQG ASATVLEETRKETAPVQLPVSGPELAAMMKIGTRVMRGVDWKWGDQDGPPPGLGRVI GELGEDGWIRVQWDTGSTNSYRMGKEGKYDLKLAELPAAAQPSAEDSDTEDDSEAEQ TERNIHPTAMMFTSTINLLQTLCLSAGVHAEIMQSEATKTLCGLLRMLVESGTTDKTSSP NRLVYREQHRSWCTLGFVRSIALTPQVCGALSSPQWITLLMKVVEGHAPFTATSLQRQI LAVHLLQAVLPSWDKTERARDMKCLVEKLFDFLGSLLTTCSSDVPLLRESTLRRRRVRP QASLTATHSSTLAEEVVALLRTLHSLTQWNGLINKYINSQLRSITHSFVGRPSEGAQLED YFPDSENPEVGGLMAVLAVIGGIDGRLRLGGQVMHDEFGEGTVTRITPKGKITVQFSDM RTCRVCPLNQLKPLPAVAFNVNNLPFTEPMLSVWAQLVNLAGSKLEKHKIKKSTKQAFA GQVDLDLLRCQQLKLYILKAGRALLSHQDKLRQILSQPAVQETGTVHTDDGAVVSPDLG DMSPEGPQPPMILLQQLLASATQPSPVKAIFDKQELEAAALAVCQCLAVESTHPSSPGF **EDCSSSEATTPVAVQHIHPARVKRRKQSPVPALPIVVQLMEMGFSRRNIEFALKSLTGA** SGNASSLPGVEALVGWLLDHSDIQVTELSDADTVSDEYSDEEVVEDVDDAAYSMSTGA VVTESQTYKKRADFLSNDDYAVYVRENIQVGMMVRCCRAYEEVCEGDVGKVIKLDRDG LHDLNVQCDWQQKGGTYWVRYIHVELIGYPPPSSSSHIKIGDKVRVKASVTTPKYKWG

.

SVTHQSVGVVKAFSANGKDIIVDFPQQSHWTGLLSEMELVPSIHPGVTCDGCQMFPING SRFKCRNCDDFDFCETCFKTKKHNTRHTFGRINEPGQSAVFCGRSGKQLKRCHSSQP GMLLDSWSRMVKSLNVSSSVNQASRLIDGSEPCWQSSGSQGKHWIRLEIFPDVLVHRL KMIVDPADSSYMPSLVVVSGGNSLNNLIELKTININPSDTTVPLLNDYTEYHRYIEIAIKQC RSSGIDCKIHGLILLGRIRAEEEDLAAVPFLASDNEEEEDEKGNSGSLIRKKAAGLESAAT IRTKVFVWGLNDKDQLGGLKGSKIKVPSFSETLSALNVVQVAGGSKSLFAVTVEGKVYA CGEATNGRLGLGISSGTVPIPRQITALSSYVVKKVAVHSGGRHATALTVDGKVFSWGEG DDGKLGHFSRMNCDKPRLIEALKTKRIRDIACGSSHSAALTSSGELYTWGLGEYGRLGH GDNTTQLKPKMVKVLLGHRVIQVACGSRDAQTLALTDEGLVFSWGDGDFGKLGRGGS **EGCNIPQNIERLNGQGVCQIECGAQFSLALTKSGVVWTWGKGDYFRLGHGSDVHVRK** PQVVEGLRGKKIVHVAVGALHCLAVTDSGQVYAWGDNDHGQQGNGTTTVNRKPTLVQ GLEGQKITRVACGSSHSVAWTTVDVATPSVHEPVLFQTARDPLGASYLGVPSDADSSA ASNKISGASNSKPNRPSLAKILLSLDGNLAKQQALSHILTALQIMYARDAVVGALMPAAMI APVECPSFSSAAPSDASAMASPMNGEECMLAVDIEDRLSPNPWQEKREIVSSEDAVTP SAVTPSAPSASARPFIPVTDDLGAASIIAETMTKTKEDVESQNKAAGPEPQALDEFTSLLI ADDTRVVVDLLKLSVCSRAGDRGRDVLSAVLSGMGTAYPQVADMLLELCVTELEDVAT DSQSGRLSSQPVVVESSHPYTDDTSTSGTVKIPGAEGLRVEFDRQCSTERRHDPLTVM DGVNRIVSVRSGREWSDWSSELRIPGDELKWKFISDGSVNGWGWRFTVYPIMPAAGP KELLSDRCVLSCPSMDLVTCLLDFRLNLASNRSIVPRLAASLAACAQLSALAASHRMWA LQRLRKLLTTEFGQSININRLLGENDGETRALSFTGSALAALVKGLPEALQRQFEYEDPI VRGGKQLLHSPFFKVLVALACDLELDTLPCCAETHKWAWFRRYCMASRVAVALDKRTP LPRLFLDEVAKKIRELMADSENMDVLHESHDIFKREQDEQLVQWMNRRPDDWTLSAG GSGTIYGWGHNHRGQLGGIEGAKVKVPTPCEALATLRPVQLIGGEQTLFAVTADGKLYA TGYGAGGRLGIGGTESVSTPTLLESIQHVFIKKVAVNSGGKHCLALSSEGEVYSWGEAE DGKLGHGNRSPCDRPRVIESLRGIEVVDVAAGGAHSACVTAAGDLYTWGKGRYGRLG HSDSEDQLKPKLVEALQGHRVVDIACGSGDAQTLCLTDDDTVWSWGDGDYGKLGRG GSDGCKVPMKIDSLTGLGVVKVECGSQFSVALTKSGAVYTWGKGDYHRLGHGSDDHV RRPRQVQGLQGKKVIAIATGSLHCVCCTEDGEVYTWGDNDEGQLGDGTTNAIQRPRLV AALQGKKVNRVACGSAHTLAWSTSKPASAGKLPAQVPMEYNHLQEIPIIALRNRLLLLH HLSELFCPCIPMFDLEGSLDETGLGPSVGFDTLRGILISQGKEAAFRKVVQATMVRDRQ HGPVVELNRIQVKRSRSKGGLAGPDGTKSVFGQMCAKMSSFGPDSLLLPHRVWKVKF VGESVDDCGGGYSESIAEICEELQNGLTPLLIVTPNGRDESGANRDCYLLSPAARAPVH SSMFRFLGVLLGIAIRTGSPLSLNLAEPVWKQLAGMSLTIADLSEVDKDFIPGLMYIRDNE ATSEEFEAMSLPFTVPSASGQDIQLSSKHTHITLDNRAEYVRLAINYRLHEFDEQVAAVR EGMARVVPVPLLSLFTGYELETMVCGSPDIPLHLLKSVATYKGIEPSASLIQWFWEVME SFSNTERSLFLRFVWGRTRLPRTIADFRGRDFVIQVLDKYNPPDHFLPESYTCFFLLKLP RYSCKQVLEEKLKYAIHFCKSIDTDDYARIALTGEPAADDSSDDSDNEDVDSFASDSTQ DYLTGH

SEQID No:50

MICTFLRAVQYTEKLHRSSAKRLLLPYIVLNKACLKTEPSLRCGLQYQKKTLRPRCILGVT QKTIWTQGPSPRKAKEDGSKQVSVHRSQRGGTAVPTSQKVKEAGRDFTYLIVVLFGISI TGGLFYTIFKELFSSSSPSKIYGRALEKCRSHPEVIGVFGESVKGYGEVTRRGRRQHVR FTEYVKDGLKHTCVKFYIEGSEPGKQGTVYAQVKENPGSGEYDFRYIFVEIESYPRRTIII EDNRSQDD

SEQID No:51

MAATSGTDEPVSGELVSVAHALSLPAESYGNDPDIEMAWAMRAMQHAEVYYKLISSVD PQFLKLTKVDDQIYSEFRKNFETLRIDVLDPEELKSESAKEKWRPFCLKFNGIVEDFNYG TLLRLDCSQGYTEENTIFAPRIQFFAIEIARNREGYNKAVYISVQDKEGEKGVNNGGEKR ADSGEEENTKNGGEKGADSGEEKEEGINREDKTDKGGEKGKEADKEINKSGEKAM

SEQID No:52

MSQRDTLVHLFAGGCGGTVGAILTCPLEVVKTRLQSSSVTLYISEVQLNTMAGASVNRV VSPGPLHCLKVILEKEGPRSLFRGLGPNLVGVAPSRAIYFAAYSNCKEKLNDVFDPDST QVHMISAAMAGFTAITATNPIWLIKTRLQLDARNRGERRMGAFECVRKVYQTDGLKGFY RGMSASYAGISETVIHFVIYESIKQKLLEYKTASTMENGEESVKEASDFVGMMLAAATSK TCATTIAYPHVVRTRLREEGTKYRSFFQTLSLLVQEEGYGSLYRGLTTHLVRQIPNTAIM MATYELVVYLLNG

SEQID No:53

MSQFKRQRINPLPGGRNFSGTASTSLLGPPPGLLTPPVATELSQNARHLQGGEKQRVF TGIVTSLHDYFGVVDEEVFFQLSVVKGRLPQLGEKVLVKAAYNPGQAVPWNAVKVQTL SNQPLLKSPAPPLLHVAALGQKQGILGAQPQLIFQPHRIPPLFPQKPLSLFQTSHTLHLS HLNRFPARGPHGRLDQGRSDDYDSKKRKQRAGGEPWGAKKPRHDLPPYRVHLTPYT VDSPICDFLELQRRYRSLLVPSDFLSVHLSWLSAFPLSQPFSLHHPSRIQVSSEKEAAPD AGAEPITADSDPAYSSKVLLLSSPGLEELYRCCMLFVDDMAEPRETPEHPLKQIKFLLGR KEEEAVLVGGEWSPSLDGLDPQADPQVLVRTAIRCAQAQTGIDLSGCTKWWRFAEFQ

YLQPGPPRRLQTVVVYLPDVWTIMPTLEEWEALCQQKAAEAAPPTQEAQGETEPTEQA
PDALEQAADTSRRNAETPEATTQQETDTDLPEAPPPPLEPAVIARPGCVNLSLHGIVED
-RRPKERISFEAGVMVLAELFLEMLQRDFGYRVYKMLLSLPEKVVSPPEPEKEEAAKEEA
TKEEEAIKEEVVKEPKDEAQNEGPATESEAPLKEDGLLPKPLSSGGEEEEKPRGEASED
LCEMALDPELLLLRDDGEEEFAGAKLEDSEVRSVASNQSEMEFSSLQDMPKELDPSAV
LPLDCLLAFVFFDANWCGYLHRRDLERILLTLGIRLSAEQAKQLVSRVVTQNICQYRSLQ
YSRQEGLDGGLPEEVLFGNLDLLPPPGKSTKPGAAPTEHKALVSHNGSLINVGSLLQRA
EQQDSGRLYLENKIHTLELKLEESHNRESATEVTNKTLAAEMQELRVRLAEAEETARTA
ERQKSQLQRLLQELRRRLTPQLEIQRVVEKADSWVEKEEPAPSN

SEQID No:54

MAPIGLKAVVGEKIMHDVIKKVKKKGEWKVLVVDQLSMRMLSSCCKMTDIMTEGITIVED INKRREPLPSLEAVYLITPSEKSVHSLISDFKDPPTAKYRAAHVFFTDSCPDALFNELVKS RAAKVIKTLTEINIAFLPYESQVYSLDSADSFQSFYSPHKAQMKNPILERLAEQIATLCATL KEYPAVRYRGEYKDNALLAQLIQDKLDAYKADDPTMGEGPDKARSQLLILDRGFDPSSP VLHELTFQAMSYDLLPIENDVYKYETSGIGEARVKEVLLDEDDDLWIALRHKHIAEVSQE VTRSLKDFSSSKRMNTGEKTTMRDLSQMLKKMPQYQKELSKYSTHLHLAEDCMKHYQ GTVDKLCRVEQDLAMGTDAEGEKIKDPMRAIVPILLDANVSTYDKIRIILLYIFLKNGITEE NLNKLIQHAQIPPEDSEIITNMAHLGVPIVTDSTLRRRSKPERKERISEQTYQLSRWTPIIK DIMEDTIEDKLDTKHYPYISTRSSASFSTTAVSARYGHWHKNKAPGEYRSGPRLIIFILGG VSLNEMRCAYEVTQANGKWEVLIGSTHILTPTKFLMDLRHPDFRESSRVSFEDQAPTM E

SEQID No:55

VAGVRPSSPHGLVGAVSVGGAGVMAVETLSPDWEFDRVDDGSQKIHAEVQLKNYGKF
LEEYTSQLRRIEDALDDSIGDVWDFNLDPIALKLLPYEQSSLLELIKTENKVLNKVITVYAA
LCCEIKKLKYEAETKFYNGLLFYGEGATDASMVEGDCQIQMGRFISFLQELSCFVTRCY
EVVMNVVHQLAALYISNKIAPKIIETTGVHFQTMYEHLGELLTVLLTLDEIIDNHITLKDHW
TMYKRLLKSVHHNPSKFGIQEEKLKPFEKFLLKLEGQLLDGMIFQACIEQQFDSLNGGVS
VSKNSTFAEEFAHSIRSIFANVEAKLGEPSEIDQRDKYVGICGLFVLHFQIFRTIDKKFYKS
LLDICKKVPAITLTANIIWFPDNFLIQKIPAAAKLLDRKSLQAIKIHRDTFLQQKAQSLTKDV
QSYYVFVSSWMMKMESILSKEQRMDKFAEDLTNRCNVFIQGFLYAYSISTIIKTTMNLYM
SMQKPMTKTSVKALCRLVELLKAIEHMFYRRSMVVADSVSHITQHLQHQALHSISVAKK
RVISDKKYSEQRLDVLSALVLAENTLNGPSTKQRRLIVSLALSVGTQMKTFKDEELFPLQ

VVMKKLDLISELRERVQTQCDCCFLYWHRAVFPIYLDDVYENAVDAARLHYMFSALRDC VPAMMHARHLESYEILLDCYDKEIMEILNEHLLDKLCKEIEKDLRLSVHTHLKLDDRNPFK VGMKDLALFFSLNPIRFFNRFIDIRAYVTHYLDKTFYNLTTVALHDWATYSEMRNLATQR YGLVMTEAHLPSQTLEQGLDVLEIMRNIHIFVSRYLYNLNNQIFIERTSNNKHLNTINIRHI ANSIRTHGTGIMNTTVNFTYQFLKKKFYIFSQFMYDEHIKSRLIKDIRFFREIKDQNDHKY PFDRAEKFNRGIRKLGITPEGQSYLDQFRQLISQIGNAMGYVRMIRSGGLHCSSNAIRFV PDLEDIVNFEELVKEEGLAEETLKAARHLDSVLSDHTRNSAEGTEYFKMLVDVFAPEFR RPKNIHLRNFYIIVPPLTLNFVEHSISCKEKLNKKNKIGAAFTDDGFAMGVAYILKLLDQYR EFDSLHWFQSVREKYLKEIRAVAKQQNVQSASQDEKLLQTMNLTQKRLDVYLQEFELL YFSLSSARIFFRADKTAAEENQEKKEKEEETKTSNGDLSDSTVSADPVVK

SEQID No:56

MRLKLFSILSTALLRATDTINSQGQFPSYLETVTKDILAPNLQWHAGRTAAAIRTAAVSCL WALTSSEVLSAEQIRDVQETLMPQVLTTLEEDSKMTRLISCRIINTFLKTSGGMTDPEKLI KIYPELLKRLDDVSNDVRMAAASTLVTWLQCVKGANAKSYYQSSVQYLYRELLVHLDDP ERAIQDAILEVLKEGSGLFPDLLVRETEAVIHKHRSATYCEQLLQHVQAVPATQ

SEQID No:57

MRNLKLFRTLEFRDIQGPGNPQCFSLRTEQGTVLIGSEHGLIEVDPVSREVKNEVSLVA **EGFLPEDGSGRIVGVQDLLDQESVCVATASGDVILCSLSTQQLECVGSVASGISVMSW** SPDQELVLLATGQQTLIMMTKDFEPILEQQIHQDDFGESKFITVGWGRKETQFHGSEGR QAAFQMQMHESALPWDDHRPQVTWRGDGQFFAVSVVCPETGARKVRVWNREFALQ STSEPVAGLGPALAWKPSGSLIASTQDKPNQQDIVFFEKNGLLHGHFTLPFLKDEVKVN DLLWNADSSVLAVRLEDLQREKSSIPKTCVQLWTVGNYHWYLKQSLSFSTCGKSKIVSL MWDPVTPYRLHVLCQGWHYLAYDWHWTTDRSVGDNSSDLSNVAVIDGNRVLVTVFR QTVVPPPMCTYQLLFPHPVNQVTFLAHPQKSNDLAVLDASNQISVYKCGDCPSADPTV KLGAVGGSGFKVCLRTPHLEKRYKIQFENNEDQDVNPLKLGLLTWIEEDVFLAVSHSEF SPRSVIHHLTAASSEMDEEHGQLNVSSSAAVDGVIISLCCNSKTKSVVLQLADGQIFKYL WESPSLAIKPWKNSGGFPVRFPYPCTQTELAMIGEEECVLGLTDRCRFFINDIEVASNIT SFAVYDEFLLLTTHSHTCQCFCLRDASFKTLQAGLSSNHVSHGEVLRKVERGSRIVTVV PQDTKLVLQMPRGNLEVVHHRALVLAQIRKWLDKLMFKEAFECMRKLRINLNPIYDHNP KVFLGNVETFIKQIDSVNHINLFFTELKEEDVTKTMYPAPVTSSVYLSRDPDGNKIDLVCD **AMRAVMESINPHKYCLSILTSHVKKTTPELEIVLQKVHELQGNAPSDPDAVSAEEALKYL** LHLVDVNELYDHSLGTYDFDLVLMVAEKSQKDPKEYLPFLNTLKKMETNYQRFTIDKYL

KRYEKAIGHLSKCGPEYFPECLNLIKDKNLYNEALKLYSPSSQQYQDISIAYGEHLMQEH MYEPAGLMFARCGAHEKALSAFLTCGNWKQALCVAAQLNFTKDQLVGLGRTLAGKLV EQRKHIDAAMVLEESAQDYEEAVLLLLEGAAWEEALRLVYKYNRLDIIETNVKPSILEAQ KNYMAFLDSQTATFSRHKKRLLVVRELKEQAQQAGLDDEVPHGQESDLFSETSSVVSG SEMSGKYSHSNSRISARSSKNRRKAERKKHSLKEGSPLEDLALLEALSEVVQNTENLKD EVYHILKVLFLFEFDEQGRELQKAFEDTLQLMERSLPEIWTLTYQQNSATPVLGPNSTAN SIMASYQQQKTSVPVLDAELFIPPKINRRTQWKLSLLD

SEQID No:58

: .

MVQKKKFCPRLLDYLVIVGARHPSSDSVAQTPELLRRYPLEDHTEFPLPPDVVFFCQPE GCLSVRQRRMSLRDDTSFVFTLTDKDTGVTRYGICVNFYRSFQKRISKGKGEGGAGSR GKEGTHATCASEEGGTESSESGSSLQPFSADSTPDVNQSPRGKRRAKAGSRSRNSTL TSLCVLSHYPFFSTFRECLYTLKRLVDCCSERLLGKKLGIPRGVQRDTMWRIFTGSLLVE EKSSALLHDLREIEAWIYRLLRSPVPVSGQKRVDIEVLPQELQPALTFALPDPSRFTLVDF PLHLPLELLGVDACLQLLTCILLEHKVVLQSRDYNALSMSVMAFVAMIYPLEYMFPVIPLL PTCMASAEQLLLAPTPYIIGVPASFFLYKLDFKMPDDVWLVDLDSNRVIAPTNAEVLPILP **EPESLELKKHLKQALASMSLNTQPILNLEKFHEGQEIPLLLGRPSNDLQSTPSTEFNPLIY** GNDADSVDVATRVAMVRFFNSANVLQGFQMHTRTLRLFPRPVVAFQAGSFLASRPRQ TPFAEKLARTQAVEYFGEWILNPTNYAFQRIHNNMFDPALIGDKPKWYAHQLQPIHYRV YDSNSQLAEALSVPPERDSDSEPTDDSGSDSMDYDDSSSSYSSLGDFVSEMMKCDIN **GDTPNVDPLTHAALGDASEVEIDELQNQKEAEEPGPDSENSQENPPLRSSSSTTASSS PSTVIHGANSEPADSTEMDDKAAVGVSKPLPSVPPSIGKSNVDRRQAEIGEGSVRRRIY** DNPYFEPQYGFPPEEDEDEQGESYTPRFSQHVSGNRAQKLLRPNSLRLASDSDAESD SRASSPNSTVSNTSTEGFGGIMSFASSLYRNHSTSFSLSNLTLPTKGAREKATPFPSLK VFGLNTLMEIVTEAGPGSGEGNRRALVDQKSSVIKHSPTVKREPPSPQGRSSNSSENQ QFLKEVVHSVLDGQGVGWLNMKKVRRLLESEQLRVFVLSKLNRMVQSEDDARQDIIPD VEISRKVYKGMLDLLKCTVLSLEQSYAHAGLGGMASIFGLLEIAQTHYYSKEPDKRKRSP TESVNTPVGKDPGLAGRGDPKAMAQLRVPQLGPRAPSATGKGPKELDTRSLKEENFIA SIELWNKHQEVKKQKALEKQRPEVIKPVFDLGETEEKKSQISADSGVSLTSSSQRTDQD SVIGVSPAVMIRSSSQDSEVSTVVSNSSGETLGADSDLSSNAGDGPGGEGSVHLASSR GTLSDSEIETNSATSTIFGKAHSLKPCIKEKLAGSPIRTSEDVSQRVYLYEGLLGRDKGS MWDQLEDAAMETFSISKERSTLWDQMQFWEDAFLDAVMLEREGMGMDQGPQEMIDR YLSLGEHDRKRLEDDEDRLLATLLHNLISYMLLMKVNKNDIRKKVRRLMGKSHIGLVYSQ QINEVLDQLANLNGRDLSIWSSGSRHMKKQTFVVHAGTDTNGDIFFMEVCDDCVVLRS

NIGTVYERWWYEKLINMTYCPKTKVLCLWRRNGSETQLNKFYTKKCRELYYCVKDSME RAAARQQSIKPGPELGGEFPVQDLKTGEGGLLQVTLEGINLKFMHNQVFIELNHIKKCNT VRGVFVLEEFVPEIKEVVSHKYKTPMAHEICYSVLCLFSYVAAVHSSEEDLRTPPRPVSS

SEQID No:59

AAASRCPGIMVALRGLGSGLQPWCPLDLRLEWVDTVWELDFTETEPLDPSIEAEIIETGL AAFTKLYESLLPFATGEHGSMESIWTFFIENNVSHSTLVALFYHFVQIVHKKNVSVQYRE YGLHAAGLYFLLLEVPGSVANQVFHPVMFDKCIQTLKKSWPQESNLNRKRKKEQPKSS QANPGRHRKRGKPPRREDIEMDEIIEEQEDENICFSARDLSQIRNAIFHLLKNFLRLPKF SLKEKPQCVQNCIEVFVSLTNFEPVLHECHVTQARALNQAKYIPELAYYGLYLLCSPIHG **EGDKVISCVFHQMLSVILMLEVGEGSHRAPLAVTSQVINCRNQAVQFISALVDELKESIF** PVVRILLQHICAKVVDKSEYRTFAAQSLVQLLSKLPCGEYAMFIAWLYKYSRSSKIPHRV FTLDVVLALLELPEREVDNTLSLEHQKFLKHKFLVQEIMFDRCLDKAPTVRSKALSSFAH CLELTVTSASESILELLINSPTFSVIESHPGTLLRNSSAFSYQRQTSNRSEPSGEINIDSSG **ETVGSGERCVMAMLRRRIRDEKTNVRKSALQVLVSILKHCDVSGMKEDLWILQDQCRD** PAVSVRKQALQSLTELLMAQPRCVQIQKAWLRGVVPVVMDCESTVQEKALEFLDQLLL QNIRHHSHFHSGDDSQVLAWALLTLLTTESQELSRYLNKAFHIWSKKEKFSPTFINNVIS HTGTEHSAPAWMLLSKIAGSSPRLDYSRIIQSWEKISSQQNPNSNTLGHILCVIGHIAKHL PKSTRDKVTDAVKCKLNGFQWSLEVISSAVDALQRLCRASAETPAEEQELLTQVCGDV LSTCEHRLSNIVLKENGTGNMDEDLLVKYIFTLGDIAQLCPARVEKRIFLLIQSVLASSAD ADHSPSSQGSSEAPASQPPPQVRGSVMPSVIRAHAIITLGKLCLQHEDLAKKSIPALVRE LEVCEDVAVRNNVIIVMCDLCIRYTIMVDKYIPNISMCLKDSDPFIRKQTLILLTNLLQEEFV KWKGSLFFRFVSTLIDSHPDIASFGEFCLAHLLKRNPVMFFQHFIECIFHFNNYEKHEKY NKFPQSEREKRLFSLKGKSNKERRMKIYKFLLEHFTDEQRFNITSKICLSILACFADGILPL DLDASELLSDTFEVLSSKEIKLLAMRSKPDKDLLMEEDDMALANVVMQEAQKKLISQVQ KRNFIENIIPIIISLKTVLEKNKIPALRELMHYLREVMQDYRDELKDFFAVDKQLASELEYD MKKYQEQLVQEQELAKHADVAGTAGGAEVAPVAQVALCLETVPVPAGQENPAMSPAV SQPCTPRASAGHVAVSSPTPETGPLQRLLPKARPMSLSTIAILNSVKKAVESKSRHRSR SLGVLPFTLNSGSPEKTCSQVSSYSLEQESNGEIEHVTKRAISTPEKSISDVTFGAGVSYI GTPRTPSSAKEKIEGRSQGNDILCLSLPDKPPPQPQQWNVRSPARNKDTPACSRRSLR KTPLKTAN

SEQID No:60

MWNDIELLTNDDTGSGYLSVGSRKEHGTALYQVDLLVKISSEKASLNPKIQACSLSDGFI

IVADQSVILLDSICRSLQLHLVFDTEVDVVGLCQEGKFLLVGERSGNLHLIHVTSKQTLLT NAFVQKANDENRRTYQNLVIEKDGSNEGTYYMLLLTYSGFFCITNLQLLKIQQAIENVDF *STAKKŁQGQIKSSFISTENYHTLGCLSLVAGDLASEVPVIIGGTGNCAFSKWEPDSSKKG MTVKNLIDAEIIKGAKKFQLIDNLLFVLDTDNVLSLWDIYTLTPVWNWPSLHVEEFLLTTE ADSPSSVTWQGITNLKLIALTASANKKMKNLMVYSLPTMEILYSLEVSSVSSLVQTGISTD TIYLLEGVCKNDPKLSEDSVSVLVLRCLTEALPENRLSRLLHKHRFAEAESFAIQFGLDV ELVYKVKSNHILEKLALSSVDASEQTEWQQLVDDAKENLHKIQDDEFVVNYCLKAQWIT YETTQEMLNYAKTRLLKKEDKTALIYSDGLKEVLRAHAKLTTFYGAFGPEKFSGSSWIEF LNNEDDLKDIFLQLKEGNLVCAQYLWLRHRANFESRFDVKMLESLLNSMSASVSLQKLC **PWFKNDVIPFVRRTVPEGQIILAKWLEQAARNLELTDKANWPENGLQLAEIFFTAEKTDE** LGLASSWHWISLKDYQNTEEVCQLRTLVNNLRELITLHRKYNCKLALSDFEKENTTTIVF RMFDKVLAPELIPSILEKFIRVYMREHDLQEEELLLLYIEDLLNRCSSKSTSLFETAWEAK AMAVIACLSDTDLIFDAVLKIMYAAVVPWSAAVEQLVKQHLEMDHPKVKLLQESYKLME MKKLLRGYGIREVNLLNKEIMRVVRYILKQDVPSSLEDALKVAQAFMLSDDEIYSLRIIDLI DREQGEDCLLLKSLPPAEAEKTAERVIIWARLALQEEPDHSKEGKAWRMSVAKTSVDI LKILCDIQKDNLQKKDECEEMLKLFKEVASLQENFEVFLSFEDYSNSSLVADLREQHIKA HEVAQAKHKPGSTPEPIAAEVRSPSMESKLHRQALALQMSKQELEAELTLRALKDGNIK TALKKCSDLFKYHCNADTGKLLFLTCQKLCQMLADNVPVTVPVGLNLPSMIHDLASQAA TICSPDFLLDALELCKHTLMAVELSRQCQMDDCGILMKASFGTHKDPYEEWSYSDFFSE DGIVLESQMVLPVIYELISSLVPLAESKRYPLESTSLPYCSLNEGDGLVLPVINSISALLQN LQESSQWELALRFVVGSFGTCLQHSVSNFMNATLSEKLFGETTLVKSRHVVMELKEKA VIFIRENATTLLHKVFNCRLVDLDLALGYCTLLPQKDVFENLWKLIDKAWQNYDKILAISLV GSELASLYQEIEMGLKFRELSTDAQWGIRLGKLGISFQPVFRQHFLTKKDLIKALVENID MDTSLILEYCSTFQLDCDAVLQLFIETLLHNTNAGQGQGDASMDSAKRRHPKLLAKALE MVPLLTSTKDLVISLSGILHKLDPYDYEMIEVVLKVIERADEKITNININQALSILKHLKSYR RISPPVDLEYQYMLEHVITLPSAAQTRLPFHLIFFGTAQNFWKILSTELSEESFPTLLLISK LMKFSLDTLYVSTAKHVFEKKLKPKLLKLTQAKSSTLINKEITKITQTIESCLLSIVNPEWAV AIAISLAQDIPEGSFKISALKFCLYLAERWLQNIPSQDEKREKAEALLKKLHIQYRRSGTEA VLIAHKLNTEEYLRVIGKPAHLIVSLYEHPSINQRIQNSSGTDYPDIHAAAKEIAEVNEINLE KVWDMLLEKWLCPSTKPGEKPSELFELQEDEALRRVQYLLLSRPIDYSSRMLFVFATST TTTLGMHQLTFAHRTRALQCLFYLADKETIESLFKKPIEEVKSYLRCITFLASFETLNIPITY ELFCSSPKEGMIKGLWKNHSHESMAVRLVTELCLEYKIYDLQLWNGLLQKLLGFNMIPY LRKVLKAISSIHSLWQVPYFSKAWQRVIQIPLLSASCPLSPDQLSDCSESLIAVLECPVSG DLDLIGVARQYIQLELPAFALACLMLMPHSEKRHQQIKNFLGSCDPQVILKQLEEHMNTG QLAGFSHQIRSLILNNIINKKEFGILAKTKYFQMLKMHAMNTNNITELVNYLANDLSLDEA SVLITEYSKHCGKPVPPDTAPCEILKMFLSGLS

SEQID No:61

MSEPGGGGGEDGSAGLEVSAVQNVADVSVLQKHLRKLVPLLLEDGGEAPAALEAALEE KSALEQMRKFLSDPQVHTVLVERSTLKEDVGDEGEEEKEFISYNINIDIHYGVKSNSLAFI KRTPVIDADKPVSSQLRVLTLSEDSPYETLHSFISNAVAPFFKSYIRESGKADRDGDKMA **PSVEKKIAELEMGLLHLQQNIEIPEISLPIHPMITNVAKQCYERGEKPKVTDFGDKVEDPT** FLNQLOSGVNRWIREIQKVTKLDRDPASGTALQEISFWLNLERALYRIQEKRESPEVLLT LDILKHGKRFHATVSFDTDTGLKQALETVNDYNPLMKDFPLNDLLSATELDKIRQALVAIF THLRKIRNTKYPIQRALRLVEAISRDLSSQLLKVLGTRKLMHVAYEEFEKVMVACFEVFQ TWDDEYEKLQVLLRDIVKRKREENLKMVWRINPAHRKLQARLDQMRKFRRQHEQLRA VIVRVLRPQVTAVAQQNQGEVPEPQDMKVAEVLFDAADANAIEEVNLAYENVKEVDGL DVSKEGTEAWEAAMKRYDERIDRVETRITARLRDQLGTAKNANEMFRIFSRFNALFVRP HIRGAIREYQTQLIQRVKDDIESLHDKFKVQYPQSQACKMSHVRDLPPVSGSIIWAKQID RQLTAYMKRVEDVLGKGWENHVEGQKLKQDGDSFRMKLNTQEIFDDWARKVQQRNL GVSGRIFTIESTRVRGRTGNVLKLKVNFLPEIITLSKEVRNLKWLGFRVPLAIVNKAHQAN QLYPFAISLIESVRTYERTCEKVEERNTISLLVAGLKKEVQALIAEGIALVWESYKLDPYV QRLAETVFNFQEKVDDLLIIEEKIDLEVRSLETCMYDHKTFSEILNRVQKAVDDLNLHSYS NLPIWVNKLDMEIERILGVRLQAGLRAWTQVLLGQAEDKAEVDMDTDAPQVSHKPGGE PKIKNVVHELRITNQVIYLNPPIEECRYKLYQEMFAWKMVVLSLPRIQSQRYQVGVHYEL TEEEKFYRNALTRMPDGPVALEESYSAVMGIVSEVEQYVKVWLQYQCLWDMQAENIY NRLGEDLNKWQALLVQIRKARGTFDNAETKKEFGPVVIDYGKVQSKVNLKYDSWHKEV LSKFGQMLGSNMTEFHSQISKSRQELEQHSVDTASTSDAVTFITYVQSLKRKIKQFEKQ VELYRNGQRLLEKQRFQFPPSWLYIDNIEGEWGAFNDIMRRKDSAIQQQVANLQMKIV QEDRAVESRTTDLLTDWEKTKPVTGNLRPEEALQALTIYEGKFGRLKDDREKCAKAKEA LELTDTGLLSGSEERVQVALEELQDLKGVWSELSKVWEQIDQMKEQPWVSVQPRKLR QNLDALLNQLKSFPARLRQYASYEFVQRLLKGYMKINMLVIELKSEALKDRHWKQLMKR LHVNWVVSELTLGQIWDVDLQKNEAIVKDVLLVAQGEMALEEFLKQAKVWNTYELDLV NYQNKCRLIRGWDDLFNKVKEHINSVSAMKLSPYYKVFEEDALSWEDKLNRIMALFDV WIDVQRRWVYLEGIFTGSADIKHLLPVETQRFQSISTEFLALMKKVSKSPLVMDVLNIQG VQRSLERLADLLGKIQKALGEYLERERSSFPRFYFVGDEDLLEIIGNSKNVAKLQKHFKK MFAGVSSIILNEDNSVVLGISSREGEEVMFKTPVSITEHPKINEWLTLVEKEMRVTLAKLL AESVTEVEIFGKATSIDPNTYITWIDKYQAQLVVLSAQIAWSENVETALSSMGGGGDAAP

LHSVLSNVEVTLNVLADSVLMEQPPLRRRKLEHLITELVHQRDVTRSLIKSKIDNAKSFE WLSQMRFYFDPKQTDVLQQLSIQMANAKFNYGFEYLGVQDKLVQTPLTDRCYLTMTQA LEARLGGSPFGPAGTGKTESVKALGHQLGRFVLVFNCDETFDFQAMGRIFVGLCQVGA WGCFDEFNRLEERMLSAVSQQVQCIQEALREHSNPNYDKTSAPITCELLNKQVKVSPD MAIFITMNPGYAGRSNLPDNLKKLFRSLAMTKPDRQLIAQVMLYSQGFRTAEVLANKIVP FFKLCDEQLSSQSHYDFGLRALKSVLVSAGNVKRERIQKIKREKEERGEAVDEGEIAEN LPEQEILIQSVCETMVPKLVAEDIPLLFSLLSDVFPGVQYHRGEMTALREELKKVCQEMY LTYGDGEEVGGMWVEKVLQLYQITQINHGLMMVGPSGSGKSMAWRVLLKALERLEGV **EGVAHIIDPKAISKDHLYGTLDPNTREWTDGLFTHVLRKIIDSVRGELQKRQWIVFDGDV** DPEWVENLNSVLDDNKLLTLPNGERLSLPPNVRIMFEVQDLKYATLATVSRCGMVWFS **EDVLSTDMIFNNFLARLRSIPLDEGEDEAQRRRKGKEDEGEEAASPMLQIQRDAATIMQ** PYFTSNGLVTKALEHAFQLEHIMDLTRLRCLGSLFSMLHQACRNVAQYNANHPDFPMQI **EQLERYIQRYLVYAILWSLSGDSRLKMRAELGEYIRRITTVPLPTAPNIPIIDYEVSISGEW** SPWQAKVPQIEVETHKVAAPDVVVPTLDTVRHEALLYTWLAEHKPLVLCGPPGSGKTM TLFSALRALPDMEVVGLNFSSATTPELLLKTFDHYCEYRRTPNGVVLAPVQLGKWLVLF CDEINLPDMDKYGTQRVISFIRQMVEHGGFYRTSDQTWVKLERIQFVGACNPPTDPGR KPLSHRFLRHVPVVYVDYPGPASLTQIYGTFNRAMLRLIPSLRTYAEPLTAAMVEFYTMS QERFTQDTQPHYIYSPREMTRWVRGIFEALRPLETLPVEGLIRIWAHEALRLFQDRLVED EERRWTDENIDTVALKHFPNIDREKAMSRPILYSNWLSKDYIPVDQEELRDYVKARLKVF YEEELDVPLVLFNEVLDHVLRIDRIFRQPQGHLLLIGVSGAGKTTLSRFVAWMNGLSVYQ **IKVHRKYTGEDFDEDLRTVLRRSGCKNEKIAFIMDESNVLDSGFLERMNTLLANGEVPG** LFEGDEYATLMTQCKEGAQKEGLMLDSHEELYKWFTSQVIRNLHVVFTMNPSSEGLKD RAATSPALFNRCVLNWFGDWSTEALYQVGKEFTSKMDLEKPNYIVPDYMPVVYDKLPQ PPSHREAIVNSCVFVHQTLHQANARLAKRGGRTMAITPRHYLDFINHYANLFHEKRSEL EEQQMHLNVGLRKIKETVDQVEELRRDLRIKSQELEVKNAAANDKLKKMVKDQQEAEK KKVMSQEIQEQLHKQQEVIADKQMSVKEDLDKVEPAVIEAQNAVKSIKKQHLVEVRSMA NPPAAVKLALESICLLLGESTTDWKQIRSIIMRENFIPTIVNFSAEEISDAIREKMKKNYMS NPSYNYEIVNRASLACGPMVKWAIAQLNYADMLKRVEPLRNELQKLEDDAKDNQQKAN **EVEQMIRDLEASIARYKEEYAVLISEAQAIKADLAAVEAKVNRSTALLKSLSAERERWEK** TSETFKNQMSTIAGDCLLSAAFIAYAGYFDQQMRQNLFTTWSHHLQQANIQFRTDIART EYLSNADERLRWQASSLPADDLCTENAIMLKRFNRYPLIIDPSGQATEFIMNEYKDRKIT RTSFLDDAFRKNLESALRFGNPLLVQDVESYDPVLNPVLNREVRRTGGRVLITLGDQDI DLSPSFVIFLSTRDPTVEFPPDLCSRVTFVNFTVTRSSLQSQCLNEVLKAERPDVDEKRS DLLKLQGEFQLRLRQLEKSLLQALNEVKGRILDDDTIITTLENLKREAAEVTRKVEETDIV

MQEVETVSQQYLPLSTACSSIYFTMESLKQIHFLYQYSLQFFLDIYHNVLYENPNLKGVT DHTQRLSIITKDLFQVAFNRVARGMLHQDHITFAMLLARIKLKGTVGEPTYDAEFQHFLR GNEIVLSAGSTPRIQGLTVEQAEAVVRLSCLPAFKDLIAKVQADEQFGIWLDSSSPEQTV PYLWSEETPATPIGQAIHRLLLIQAFRPDRLLAMAHMFVSTNLGESFMSIMEQPLDLTHIV GTEVKPNTPVLMCSVPGYDASGHVEDLAAEQNTQITSIAIGSAEGFNQADKAINTAVKS GRWVMLKNVHLAPGWLMQLEKKLHSLQPHACFRLFLTMEINPKVPVNLLRAGRIFVFEP PPGVKANMLRTFSSIPVSRICKSPNERARLYFLLAWFHAIIQERLRYAPLGWSKKYEFGE SDLRSACDTVDTWLDDTAKASGRQNISPDKIPWSALKTLMAQSIYGGRVDNEFDQRLL NTFLERLFTTRSFDSEFKLACKVDGHKDIQMPDGIRREEFVQWVELLPDTQTPSWLGLP NNAERVLLTTQGVDMISKMLKMQMLEDEDDLAYAETEKKTRTDSTSDGRPAWMRTLH TTASNWLHLIPQTLSHLKRTVENIKDPLFRFFEREVKMGAKLLQDVRQDLADVVQVCEG KKKQTNYLRTLINELVKGILPRSWSHYTVPAGMTVIQWVSDFSERIKQLQNISLAAASGG AKELKNIHVCLGGLFVPEAYITATRQYVAQANSWSLEELCLEVNVTTSQGATLDACSFG VTGLKLQGATCNNNKLSLSNAISTALPLTQLRWVKQTNTEKKASVVTLPVYLNFTRADLI FTVDFEIATKEDPRSFYERGVAVLCTE

SEQID No:62

MQSRLLLLGAPGGHGGPASRRMRLLLRQVVQRRPGGDRQRPEVRLLHAGSGADTGD TVNIGDVSYKLKIPKNPELVPQNYISDSLAQSVVQHLRWIMQKDLLGQDVFLIGPPGPLR RSIAMQYLELTKREVEYIALSRDTTETDLKQRREIRAGTAFYIDQCAVRAATEGRTLILEG LEKAERNVLPVLNNLLENREMQLEDGRFLMSAERYDKLLRDHTKKELDSWKIVRVSENF RVIALGLPVPRYSGNPLDPPLRSRFQARDIYYLPFKDQLKLLYSIGANVSAEKVSQLLSF ATTLCSQESSTLGLPDFPLDSLAAAVQILDSFPMMPIKHAIQWLYPYSILLGHEGKMAVE GVLKRFELQDSGSSLLPKEIVKVEKMMENHVSQASVTIRIADKEVTIKVPAGTRLLSQPC ASDRFIQTLSHKQLQAEMMQSHMVKDICLIGGKGCGKTVIAKNFADTLGYNIEPIMLYQD MTARDLLQQRYTLPNGDTAWRSSPLVNAALEGKLVLLDGIHRVNAGTLAVLQRLIHDRE LSLYDGSRLLREDRYMRLKEELQLSDEQLQKRSIFPIHPSFRIIALAEPPVIGSTAHQWLG PEFLTMFFFHYMKPLVKSEEIQVIKEKVPNVPQEALDKLLSFTHKLRETQDPTAQSLAAS LSTRQLLRISRRLSQYPNENLHSAVTKACLSRFLPSLARSALEKNLADATIEINTDDNLEP ELKDYKCEVTSGTLRIGAVSAPIYNAHEKMKVPDVLFYDNIQHVIVMEDMLKDFLLGEHL LLVGNQGVGKNKIVDRFLHLLNRPREYIQLHRDTTVQTLTLQPSVKDGLIVYEDSPLVKA VKLGHILVVDEADKAPTNVTCILKTLVENGEMILADGRRIVANSANVNGRENVVVIHPDF RMIVLANRPGFPFLGNDFFGTLGDIFSCHAVDNPKPHSELEMLRQYGPNVPEPILQKLV **AAFGELRSLADQGIINYPYSTREVVNIVKHLQKFPTEGLSSVVRNVFDFDSYNNDMREILI**

NTLHKYGIPIGAKPTSVQLAKELTLPEQTFMGYWTIGQARSGMQKLLCPVETHHIDIKGP ALINIQEYPIERHEERSLNFTEECASWRIPLDEINIICDIATSHENEQNTLYVVTCNPASLYF MNMTGKSGFFVDFFDIFPRTANGVWHPFVTVAPLGSPLKGQVVLHEQQSNVILLLDTTG RALHRLILPSEKFTSKKPFWWNKEEAETYKMCKEFSHKNWLVFYKEKGNSLTVLDVLE GRTHTISLPINLKTVFLVAEDKWLLVESKTNQKYLLTKPAHIESEGSGVCQLYVLKEEPPS TGFGVTQETEFSIPHKISSDQLSSEHLSSAVEQKIASPNRILSDEKNYATIVVGFPDLMSP SEVYSWKRPSSLHKRSGTDTSFYRGKKKRGTPKQSNCVTLLDTNQVVRILPPGEVPLK DIYPKDVTPPQTSGYIEVTDLQSKKLRYIPIPRSESLSPYTTWLSTISDTDALLAEWDKSG VVTVDMGGHIRLWETGLERLQRSLMEWRNMIGQDDRNMQITINRDSGEDVSSPKHGK EDPDNMPHVGGNTWAGGTGGRDTAGLGGKGGPYRLDAGHTVYQVSQAEKDAVPEE VKRAAREMGQRAFQQRLKEIQMSEYDAATYERFSGAVRRQVHSLRIILDNLQAKGKER QWLRHQATGELDDAKIIDGLTGEKAIYKRRGELEPQLGSPQQKPKRLRLVVDVSGSMY RFNRMDGRLERTMEAVCMVMEAFENYEEKFQYDIVGHSGDGYNIGLVPMNKIPKDNK QRLEILKTMHAHSQFCMSGDHTLEGTEHAIKEIVKEEADEYFVIVLSDANLSRYGIHPAKF AQILTRDPQVNAFAIFIGSLGDQATRLQRTLPAGRSFVAMDTKDIPQILQQIFTSTMLSSV

SEQID No:63

MLERKYGGRLVTRHAARTIQTAFRQYQMNKNFERLRSSMSENRMSRRIVLSNMRMQF
SFEGPEKVHSSYFEGKQVSVTNDGSQLGALVSPECGDLSEPTTLKSPAPSSDFADAITE
LEDAFSRQVKSLAESIDDALNCRSLHTEEAPALDAARARDTEPQTALHGMDHRKLDEM
TASYSDVTLYIDEEELSPPLPLSQAGDRPSSTESDLRLRAGGAAPDYWALAHKEDKADT
DTSCRSTPSLERQEQRLRVEHLPLLTIEPPSDSSVDLSDRSERGSLKRQSAYERSLGG
QQGSPKHGPHSGAPKSLPREEPELRPRPPRPLDSHLAINGSANRQSKSESDYSDGDN
DSINSTSNSNDTINCSSESSSRDSLREQTLSKQTYHKEARNSWDSPAFSNDVIRKRHYR
IGLNLFNKKPEKGVQYLIERGFVPDTPVGVAHFLLQRKGLSRQMIGEFLGNRQKQFNRD
VLDCVVDEMDFSTMELDEALRKFQAHIRVQGEAQKVERLIEAFSQRYCICNPGVVRQFR
NPDTIFILAFAIILLNTDMYSPNVKPERKMKLEDFIKNLRGVDDGEDIPREMLMGIYERIRK
RELKTNEDHVSQVQKVEKLIVGKKPIGSLHPGLGCVLSLPHRRLVCYCRLFEVPDPNKP
QKLGLHQREIFLFNDLLVVTKIFQKKKNSVTYSFRQSFSLYGMQVLLFENQYYPNGIRLT
SSVPGADIKVLINFNAPNPQDRKKFTDDLRESIAEVQEMEKHRIESELEKQKGVVRPSM
SQCSSLKKESGNGTLSRACLDDSYASGEGLKRSALSSSLRDLSEAGKRGRRSSAGSLE
SNVEFQPFEPLQPSVLCS

SEQID No:64

MPLKHYLLLLVGCQAWGAGLAYHGCPSECTCSRASQVECTGARIVAVPTPLPWNAMS LQILNTHITELNESPFLNISALIALRIEKNELSRITPGAFRNLGSLRYLSLANNKLQVLPIGLF QGLDSLESLLLSSNQLLQIQPAHFSQCSNLKELQLHGNHLEYIPDGAFDHLVGLTKLNLG KNSLTHISPRVFQHLGNLQVLRLYENRLTDIPMGTFDGLVNLQELALQQNQIGLLSPGLF HNNHNLQRLYLSNNHISQLPPSIFMQLPQLNRLTLFGNSLKELSLGIFGPMPNLRELWLY DNHISSLPDNVFSNLRQLQVLILSRNQISFISPGAFNGLTELRELSLHTNALQDLDGNVFR MLANLQNISLQNNRLRQLPGNIFANVNGLMAIQLQNNQLENLPLGIFDHLGKLCELRLYD NPWRCDSDILPLRNWLLLNQPRLGTDTVPVCFSPANVRGQSLIIINVNVAVPSVHVPEVP SYPETPWYPDTPSYPDTTSVSSTTELTSPVEDYTDLTTIQVTDDRSVWGMTHAHSGLAI AAIVIGIVALACSLAACVGCCCCKKRSQAVLMQMKAPNEC

SEQID No:65

MRGSHRAAPALRPRGRLWPVLAVLAAAAAAGCAQAAMDECTDEGGRPQRCMPEFVN AAFNVTVVATNTCGTPPEEYCVQTGVTGVTKSCHLCDAGQPHLQHGAAFLTDYNNQA DTTWWQSQTMLAGVQYPSSINLTLHLGKAFDITYVRLKFHTSRPESFAIYKRTREDGPW IPYQYYSGSCENTYSKANRGFIRTGGDEQQALCTDEFSDFSPLTGGNVAFSTLEGRPS AYNFDNSPVLQEWVTATDIRVTLNRLNTFGDEVFNDPKVLKSYYYAISDFAVGGRCKCN GHASECMKNEFDKLVCNCKHNTYGVDCEKCLPFFNDRPWRRATAESASECLPCDCNG RSQECYFDPELYRSTGHGGHCTNCQDNTDGAHCERCRENFFRLGNNEACSSCHCSP VGSLSTQCDSYGRCSCKPGVMGDKCDRCQPGFHSLTEAGCRPCSCDPSGSIDECNV **ETGRCVCKDNVEGFNCERCKPGFFNLESSNPRGCTPCFCFGHSSVCTNAVGYSVYSIS** STFQIDEDGWRAEQRDGSEASLEWSSERQDIAVISDSYFPRYFIAPAKFLGKQVLSYGQ NLSFSFRVDRRDTRLSAEDLVLEGAGLRVSVPLIAQGNSYPSETTVKYVFRLHEATDYP WRPALTPFEFQKLLNNLTSIKIRGTYSERSAGYLDDVTLASARPGPGVPATWVESCTCP VGYGGQFCEMCLSGYRRETPNLGPYSPCVLCACNGHSETCDPETGVCNCRDNTAGP HCEKCSDGYYGDSTAGTSSDCQPCPCPGGSSCAVVPKTKEVVCTNCPTGTTGKRCEL CDDGYFGDPLGRNGPVRLCRLCQCSDNIDPNAVGNCNRLTGECLKCIYNTAGFYCDR CKDGFFGNPLAPNPADKCKACNCNPYGTMKQQSSCNPVTGQCECLPHVTGQDCGAC DPGFYNLQSGQGCERCDCHALGSTNGQCDIRTGQCECQPGITGQHCERCEVNHFGF GPEGCKPCDCHPEGSLSLQCKDDGRCECREGFVGNRCDQCEENYFYNRSWPGCQE **CPACYRLVKDKVADHRVKLQELESLIANLGTGDEMVTDQAFEDRLKEAEREVMDLLRE** AQDVKDVDQNLMDRLQRVNNTLSSQISRLQNIRNTIEETGNLAEQARAHVENTERLIEIA SRELEKAKVAAANVSVTQPESTGDPNNMTLLAEEARKLAERHKQEADDIVRVAKTAND

TSTEAYNLLLRTLAGENQTAFEIEELNRKYEQAKNISQDLEKQAARVHEEAKRAGDKAV EIYASVAQLSPLDSETLENEANNIKMEAENLEQLIDQKLKDYEDLREDMRGKELEVKNLL EKGKTEQQTADQLLARADAAKALAEEAAKKGRDTLQEANDILNNLKDFDRRVNDNKTA AEEALRKIPAINQTITEANEKTREAQQALGSAAADATEAKNKAHEAERIASAVQKNATST KAEAERTFAEVTDLDNEVNNMLKQLQEAEKELKRKQDDADQDMMMAGMASQAAQEA EINARKAKNSVTSLLSIINDLLEQLGQLDTVDLNKLNEIEGTLNKAKDEMKVSDLDRKVSD LENEAKKQEAAIMDYNRDIEEIMKDIRNLEDIRKTLPSGCFNTPSIEKP

SEQID No:66

MAAATEHNRPSSGDRNLERRCSPNLSREVLYEIFRSLHTLVGQLDLRDDVVKITIDWNK LQSLSAFQPALLFSALEQHILYLQPFLAKLQSPIKEENTTAVEEIGRTEMGNKNEVNDKF SIGDLQEEEKHKESDLRDVKKTQIHFDPEVVQIKAGKAEIDRRISAFIERKQAEINENNVR EFCNVIDCNQENSCARTDAIFTPYPGFKSHVKVSRVVNTYGPQTRPEGIPGSGHKPNS MLRDCGNQAVEERLQNIEAHLRLQTGGPVPRDIYQRIKKLEDKILELEGISPEYFQSVSF SGKRRKVQPPQQNYSLAELDEKISALKQALLRKSREAESMATHHLP

SEQID No:67

LCNGVNDCGDNSDESPQQNCRPRTGEENCNVNNGGCAQKCQMVRGAVQCTCHTGY RLTEDGHTCQDVNECAEEGYCSQGCTNSEGAFQCWCETGYELRPDRRSCKALGPEP VLLFANRIDIRQVLPHRSEYTLLLNNLENAIALDFHHRRELVFWSDVTLDRILRANLNGSN VEEVVSTGLESPGGLAVDWVHDKLYWTDSGTSRIEVANLDGAHRKVLLWQNLEKPRAI ALHPMEGTIYWTDWGNTPRIEASSMDGSGRRIIADTHLFWPNGLTIDYAGRRMYWVDA KHHVIERANLDGSHRKAVISQGLPHPFAITVFEDSLYWTDWHTKSINSANKFTGKNQEII RNKLHFPMDIHTLHPQRQPAGKNRCGDNNGGCTHLCLPSGQNYTCACPTGFRKISSH ACAQSLDKFLLFARRMDIRRISFDTEDLSDDVIPLADVRSAVALDWDSRDDHVYWTDVS TDTISRAKWDGTGQEVVVDTSLESPAGLAIDWVTNKLYWTDAGTDRIEVANTDGSMRT VLIWENLDRPRDIVVEPMGGYMYWTDWGASPKIERAGMDASGRQVIISSNLTWPNGLA IDYGSQRLYWADAGMKTIEFAGLDGSKRKVLIGSQLPHPFGLTLYGERIYWTDWQTKSI QSADRLTGLDRETLQENLENLMDIHVFHRRRPPVSTPCAMENGGCSHLCLRSPNPSGF SCTCPTGINLLSDGKTCSPGMNSFLIFARRIDIRMVSLDIPYFADVVVPINITMKNTIAVGV DPQEGKVYWSDSTLHRISRANLDGSQHEDIITTGLQTTDGLAVDAIGRKVYWTDTGTNR **IEVGNLDGSMRKVLVWQNLDSPRAIVLYHEMGFMYWTDWGENAKLERSGMDGSDRA** VLINNNLGWPNGLTVDKASSQLLWADAHTERIEAADLNGANRHTLVSPVQHPYGLTLLD SYIYWTDWQTRSIHRADKGTGSNVILVRSNLPGLMDMQAVDRAQPLGFNKCGSRNGG

CSHLCLPRPSGFSCACPTGIQLKGDGKTCDPSPETYLLFSSRGSIRRISLDTSDHTDVHV
PVPELNNVISLDYDSVDGKVYYTDVFLDVIRRADLNGSNMETVIGRGLKTTDGLAVDWV
ARNLYWTDTGRNTIEASRLDGSCRKVLINNSLDEPRAIAVFPRKGYLFWTDWGHIAKIER
ANLDGSERKVLINTDLGWPNGLTLDYDTRRIYWVDAHLDRIESADLNGKLRQVLVGHVS
HPFALTQQDRWIYWTDWQTKSIQRVDKYSGRNKETVLANVEGLMDIIVVSPQRQTGTN
ACGVNNGGCTHLCFARASDFVCACPDEPDSQPCSLVPGLVPPAPRATGMSEKSPVLP
NTPPTTLYSSTTRTRTSLEEVEGRCSERDARLGLCARSNDAVPAAPGEGLHISYAIGGL
LSILLILVVIAALMLYRHKKSKFTDPGMGNLTYSNPSYRTSTQEVKIEAIPKPAMYNQLCY
KKEGGPDHNYTKEKIKIVEGICLLSGDDAEWDDLKQLRSSRGGLLRDHVCMKTDTVSIQ
ASSGSLDDTEMEQLLQEEQSECSSVHTAATPERRGSLPDTGWKHERKLSSESQV

SEQID No:68

MRRAPCVRDKLREIVGASTNWRDHVKAMEERKLLHSFLAKSQDGLPPRRMKDSYIEVL LPLGSEPELREKYLTVQNTVRFGRILEDLDSLGVLICYMHNKIHSAKMSPLSIVTALVDKI DMCKKSLSPEQDIKFSGHVSWVGKTSMEVKMQMFQLHGDEFCPVLDATFVMVARDSE NKGPAFVNPLIPESPEEEELFRQGELNKGRRIAFSSTSLLKMAPSAEERTTIHEMFLSTL DPKTISFRSRVLPSNAVWMENSKLKSLEICHPQERNIFNRIFGGFLMRKAYELAWATAC SFGGSRPFVVAVDDIMFQKPVEVGSLLFLSSQVCFTQNNYIQVRVHSEVASLQEKQHTT TNVFHFTFMSEKEVPLVFPKTYGESMLYLDGQRHFNSMSGPATLRKDYLVEP

SEQID No:69

MSVKEAGSSGRREQAAYHLHIYPQLSTTESQASCRVTATKDSTTSDVIKDAIASLRLDG
TKCYVLVEVKESGGEEWVLDANDSPVHRVLLWPRRAQDEHPQEDGYYFLLQERNADG
TIKYVHMQLVAQATATRRLVERGLLPRQQADFDDLCNLPELTEGNLLKNLKHRFLQQKI
YTYAGSILVAINPFKFLPIYNPKYVKMYENQQLGKLEPHVFALADVAYYTMLRKRVNQCI
VYPGESGSGKTQSTNFLIHCLTALSQKGYASGVERTILGACPVLEAFGNAKTAHNNNSS
RFGKFIQVSYLESGIVRGAVVEKYLLEKSRLVSQEKDERNYHVFYYLLLGVSEEERQEF
QLKQPEDYFYLNQHNLKIEDGEDLKHDFERLKQAMEMVGFLPATKKQIFAVLSAILYLGN
VTYKKRATGREEGLEVGPPEVLDTLSQLLKVKREILVEVLTKRKTVTVNDKLILPYSLSEA
ITARDSMAKSLYSALFDWIVLRINHALLNKKDVEEAVSCLSIGVLDIFGFEDFERNSFEQF
CINYANEQLQYYFNQHIFKLEQEEYQGEGITWHNIGYTDNVGCIHLISKKPTGLFYLLDEE
SNFPHATSQTLLAKFKQQHEDNKYFLGTPVMEPAFIIQHFAGKVKYQIKDFREKNMDYM
RPDIVALLRGSDSSYVRELIGMDPVAVFRWAVLRAAIRAMAVLREAGRLRAERAEKAAG
MSSPGAQSHPEELPRGASTPSEKLYRDLHNQMIKSIKGLPWQGEDPRSLLQSLSRLQK

PRAFILKSKGIKQKQIIPKNLLDSKSLKLIISMTLHDRTTKSLLHLHKKKKPPSISAQFQTSL NKLLEALGKAEPFFIRCIRSNAEKKELCFDDELVLQQLRYTGMLETVRIRRSGYSAKYTF **QDETEQFQVLLPKDAQPCREVISTLLEKMKIDKRNYQIGKTKVFLKETERQALQETLHRE** VVRKILLLQSWFRMVLERRHFLQMKRAAVTIQACWRSYRVRRALERTQAAVYLQAAWR GYWQRKLYRHQKQSIIRLQSLCRGHLQRKSFSQMISEKQKAEEKEREALEAARAGAEE GGQGQAAGGQQVAEQGPEPAEDGGHLASEPEVQPSDRSPLEHSSPEKEAPSPEKTL PPQKTVAAESHEKVPSSREKRESRRQRGLEHVKFQNKHIQSCKEESALREPSRRVTQE QGVSLLEDKKESREDETLLVVETEAENTSQKQPTEQPQAMAVGKVSEETEKTLPSGSP RPGQLERPTSLALDSRVSPPAPGSAPETPEDKSKPCGSPRVQEKPDSPGGSTQIQRYL DAERLASAVELWRGKKLVAAASPSAMLSQSLDLSDRHRATGAALTPTEERRTSFSTSD VSKLLPSLAKAQPAAETTDGERSAKKPAVQKKKPGDASSLPDAGLSPGSQVDSKSTFK RLFLHKTKDKKYSLEGAEELENAVSGHVVLEATTMKKGLEAPSGQQHRHAAGEKRTKE PGGKGKKNRNVKIGKITVSEKWRESVFRQITNANELKYLDEFLLNKINDLRSQKTPIESLF **IEATEKFRSNIKTMYSVPNGKIHVGYKDLMENYQIVVSNLATERGQKDTNLVLNLFQSLL** DEFTRGYTKNDFEPVKQSKAQKKKRKQERAVQEHNGHVFASYQVSIPQSCEQCLSYIW LMDKALLCSVCKMTCHKKCVHKIQSHCSYTYGRKGEPGAEPGHFGVCVDSLTSDKASV PIVLEKLLEHVEMHGLYTEGLYRKSGAANRTRELRQALQTDPAAVKLENFPIHAITGVLK QWLRELPEPLMTFAQYGDFLRAVELPEKQEQLAAIYAVLEHLPEANHNSLERLIFHLVKV ALLEDVNRMSPGALAIIFAPCLLRCPDNSDPLTSMKDVLKITTCVEMLIKEQMRKYKVKM **EEISQLEAAESIAFRRLSLLRQNANKSPKTREPAGGAGRLLTTSRVSPSPSTRNLALGS** WRSAALRTRGTGRPARPGRARALRRRPPRPARESPAQPPRSRPRVRTETPSPLSSGP **PPSRSNTGMAPLRR**

SEQID No:70

MTGERPSTALPDRRWGPRILGFWGGCRVWVFAAIFLLLSLAASWSKAENDFGLVQPLV
TMEQLLWVSGRQIGSVDTFRIPLITATPRGTLLAFAEARKMSSSDEGAKFIALRRSMDQ
GSTWSPTAFIVNDGDVPDGLNLGAVVSDVETGVVFLFYSLCAHKAGCQVASTMLVWSK
DDGVSWSTPRNLSLDIGTEVFAPGPGSGIQKQREPRKGRLIVCGHGTLERDGVFCLLS
DDHGASWRYGSGVSGIPYGQPKQENDFNPDECQPYELPDGSVVINARNQNNYHCHC
RIVLRSYDACDTLRPRDVTFDPELVDPVVAAGAVVTSSGIVFFSNPAHPEFRVNLTLRW
SFSNGTSWRKETVQLWPGPSGYSSLATLEGSMDGEEQAPQLYVLYEKGRNHYTESIS
VAKISVYGTL

SEQID No:71

MAPRICSISVTARRILGGPGPRAGDVASAAAARFYSKDNEGSWFRSLFVHKVDPRKDA HSTLLSKKETSNLYKIQFHNVKPEYLDAYNSLTEAVLPKLHLDEDYPCSLVGNWNTWYG EQDQAVHLWRFSGGYPALMDCMNKLKNNKEYLEFRRERSQMLLSRRNQLLLEFSFWN EPQPRMGPNIYELRTYKLKPGTMIEWGNNWARAIKYRQENQEAVGGFFSQIGELYVVH HLWAYKDLQSREETRNAAWRKRGWDENVYYTVPLVRHMESRIMIPLKISPLQ

SEQID No:72

MAARVLRARGAAWAGGLLQRAAPCSLLPRLRTWTSSSNRSREDSWLKSLFVRKVDPR KDAHSNLLAKKETSNLYKLQFHNVKPECLEAYNKICQEVLPKIHEDKHYPCTLVGTWNT WYGEQDQAVHLWRYEGGYPALTEVMNKLRENKEFLEFRKARSDMLLSRKNQLLLEFS FWNEPVPRSGPNIYELRSYQLRPGTMIEWGNYWARAIRFRQDGNEAVGGFFSQIGQLY MVHHLWAYRDLQTREDIRNAAWHKHGWEELVYYTVPLIQEMESRIMIPLKTSPLQ

SEQID No:73

MGTALLQRGGCFLLCLSLLLLGCWAELGSGLEFPGAEGQWTRFPKWNACCESEMSFQ LKTRSARGLVLYFDDEGFCDFLELILTRGGRLQLSFSIFCAEPATLLADTPVNDGAWHSV RIRRQFRNTTLFIDQVEAKWVEVKSKRRDMTVFSGLFVGGLPPELRAAALKLTLASVRE REPFKGWIRDVRVNSSQVLPVDSGEVKLDDEPPNSGGGSPCEAGEEGEGGVCLNGG VCSVVDDQAVCDCSRTGFRGKDCSQEDNNVEGLAHLMMGDQGKSKGKEEYIATFKG SEYFCYDLSQNPIQSSSDEITLSFKTLQRNGLMLHTGKSADYVNLALKNGAVSLVINLGS GAFEALVEPVNGKFNDNAWHDVKVTRNLRQHSGIGHAMVTISVDGILTTTGYTQEDYT. MLGSDDFFYVGGSPSTADLPGSPVSNNFMGCLKEVVYKNNDVRLELSRLAKQGDPKM KIHGVVAFKCENVATLDPITFETPESFISLPKWNAKKTGSISFDFRTTEPNGLILFSHGKP RHQKDAKHPQMIKVDFFAIEMLDGHLYLLLDMGSGTIKIKALLKKVNDGEWYHVDFQRD GRSGTISVNTLRTPYTAPGESEILDLDDELYLGGLPENKAGLVFPTEVWTALLNYGYVG CIRDLFIDGQSKDIRQMAEVQSTAGVKPSCSKETAKPCLSNPCKNNGMCRDGWNRYV CDCSGTGYLGRSCEREATVLSYDGSMFMKIQLPVVMHTEAEDVSLRFRSQRAYGILMA TTSRDSADTLRLELDAGRVKLTVNLDCIRINCNSSKGPETLFAGYNLNDNEWHTVRVVR RGKSLKLTVDDQQAMTGQMAGDHTRLEFHNIETGIITERRYLSSVPSNFIGHLQSLTFN GMAYIDLCKNGDIDYCELNARFGFRNIIADPVTFKTKSSYVALATLQAYTSMHLFFQFKT TSLDGLILYNSGDGNDFIVVELVKGYLHYVFDLGNGANLIKGSSNKPLNDNQWHNVMIS RDTSNLHTVKIDTKITTQITAGARNLDLKSDLYIGGVAKETYKSLPKLVHAKEGFQGCLAS VDLNGRLPDLISDALFCNGQIERGCEGPSTTCQEDSCSNQGVCLQQWDGFSCDCSMT

SFSGPLCNDPGTTYIFSKGGGQITYKWPPNDRPSTRADRLAIGFSTVQKEAVLVRVDSS SGLGDYLELHIHQGKIGVKFNVGTDDIAIEESNAIINDGKYHVVRFTRSGGNATLQVDSW PVIERYPAGRQLTIFNSQATIIIGGKEQGQPFQGQLSGLYYNGLKVLNMAAENDANIAIVG NVRLVGEVPSSMTTESTATAMQSEMSTSIMETTTTLATSTARRGKPPTKEPISQTTDDIL VASAECPSDDEDIDPCEPSSGGLANPTRAGGREPYPGSAEVIRESSSTTGMVVGIVAAA ALCILILLYAMYKYRNRDEGSYHVDESRNYISNSAQSNGAVVKEKQPSSAKSSNKNKKN KDKEYYV

SEQID No:74

MTTQQIDLQGPGPWGFRLVGGKDFEQPLAISRVTPGSKAALANLCIGDVITAIDGENTS
NMTHLEAQNRIKGCTDNLTLTVARSEHKVWSPLVTEEGKRHPYKMNLASEPQEVLHIG
SAHNRSAMPFTASPASSTTARVITNQYNNPAGLYSSENISNFNNALESKTAASGVEANS
RPLDHAQPPSSLVIDKESEVYKMLQEKQELNEPPKQSTSFLVLQEILESEEKGDPNKPS
GFRSVKAPVTKVAASIGNAQKLPMCDKCGTGIVGVFVKLRDRHRHPECYVCTDCGTNL
KQKGHFFVEDQIYCEKHARERVTPPEGYEVVTVFPK

SEQID No:75

MGAGAETGRGQRAAAPERRHGRLLWLLRGLTLGTAPRRAVRGQAGGGGPGTAGIVG EAGSLATCELPLAKSEWQKKLTPEQFYVTREKGTEPPFSGIYLNNKEAGMYHCVCCDS PLFSSEKKYCSGTGWPSFSEAHGTSGSDESHTGILRRLDTSLGSARTEVVCKQCEAHL GHVFPDGPGPNGQRFCINSVALKFKPRKH

SEQID No:76

MTSAAPAKKPYRKAPPEHRELRLEIPGSRLEQEEPLTDAERMKLLQEENEELRRRLASA
TRRTEALERELEIGQDCLELELGQSREELDKFKDKFRRLQNSYTASQRTNQELEDKLHT
LIKKAEMDRKTLDWEIVELTNKLLDAKNTINKLEELNERYRLDCNPAVQLLKCNKSHFRN
HKFADLPCELQDMVRKHLHSGQEAASPGPAPSLAPGAVVPTSVIARVLEKPESLLLNSA
QSGSAGRPLAEDVFVHVDMSEGVPGDPASPPAPGSPTPQPNGECHSLGTARGSPEEE
LPLPAFEKLNPYPTPSPPHPLYPGRRVIEFSEDKVRIPRNSPLPNCTYATRQAISLSLVEE
GSERARPSPVPSTPASAQASPHHQPSPAPLTLSAPASSASSEEDLLVSWQRAFVDRTP
PPAAVAQRTAFGRDALPELQRHFAHSPADRDEVVQAPSARPEESELLLPTEPDSGFPR
EEEELNLPISPEEERQSLLPINRGTEEGPGTSHTEGRAWPLPSSSRPQRSPKRMGVHH
LHRKDSLTQAQEQGNLLN

SEQID No:77

MGTTASTAQQTVSAGTPFEGLQGSGTMDSRHSVSIHSFQSTSLHNSKAKSIIPNKVAPV VITYNCKEEFQIHDELLKAHYTLGRLSDNTPEHYLVQGRYFLVRDVTEKMDVLGTVGSC GAPNFRQVQGGLTVFGMGQPSLSGFRRVLQKLQKDGHRECVIFCVREEPVLFLRADE DFVSYTPRDKQNLHENLQGLGPGVRVESLELAIRKEIHDFAQLSENTYHVYHNTEDLWG EPHAVAIHGEDDLHVTEEVYKRPLFLQPTYRYHRLPLPEQGSPLEAQLDAFVSVLRETP SLLQLRDAHGPPPALVFSCQMGVGRTNLGMVLGTLILLHRSGTTSQPEAAPTQAKPLP MEQFQVIQSFLRMVPQGRRMVEEVDRAITACAELHDLKEVVLENQKKLEGIRPESPAQ GSGSRHSVWQRALWSLERYFYLILFNYYLHEQYPLAFALSFSRWLCAHPELYRLPVTLS SAGPVAPRDLIARGSLREDDLVSPDALSTVREMDVANFRRVPRMPIYGTAQPSAKALG SILAYLTDAKRRLRKVVWVSLREEAVLECDGHTYSLRWPGPPVAPDQLETLEAQLKAHL SEPPPGKEGPLTYRFQTCLTMQEVFSQHRRACPGLTYHRIPMPDFCAPREEDFDQLLE ALRAALSKDPGTGFVFSCLSGQGRTTTAMVVAVLAFWHIQGFPEVGEEELVSVPDAKF TKGEFQVVMKVVQLLPDGHRVKKEVDAALDTVSETMTPMHYHLREIIICTYRQAKAAKE AQEMRRLQLRSLQYLERYVCLILFNAYLHLEKADSWQRPFSTWMQEVASKAGIYEILNE LGFPELESGEDQPFSRLRYRWQEQSCSLEPSAPEDLL

SEQID No:78

MAALYRPGLRLNWHGLSPLGWPSCRSIQTLRVLSGDLGQLPTGIRDFVEHSARLCQPE GIHICDGTEAENTATLTLLEQQGLIRKLPKYNNCWLARTDPKDVARVESKTVIVTPSQRD TVPLPPGGARGQLGNWMSPADFQRAVDERFPGCMQGRTMYVLPFSMGPVGSPLSRI GVQLTDSAYVVASMRIMTRLGTPVLQALGDGDFVKCLHSVGQPLTGQGEPVSQWPCN PEKTLIGHVPDQREIISFGSGYGGNSLLGKKCFALRIASRLARDEGWLAEHMLILGITSPA GKKALCAAAFPSACGKTNLAMMRPALPGWKVECVGDDIAWMRFDSEGRLRAINPENG FFGVAPGTSATTNPNAMATIQSNTIFTNVAETSDGGVYWEGIDQPLPPGVTVTSWLGKP WKPGDKEPCAHPNSRFCAPARQCPIMDPAWEAPEGVPIDAIIFGGRRPKGVPLVYEAF NWRHGVFVGRAMRSESTAAAEHKGKIIMHDPFAMRPFFGYNFGHYLEHWLSMEGRKG AQLPRIFHVNWFRRDEAGHFLWPGFGENARVLDWICRRLEGEDSARETPIGLVPKEGA LDLSGLRAIDTTQLFSLPKDFWEQEVRDIRSYLTEQVNQDLPKEVLAELEALERRVHKM

SEQID No:79

MLPAATASLLGPLLTACALLPFAQGQTPNYTRPVFLCGGDVKGESGYVASEGFPNLYP PNKECIWTITVPEGQTVSLSFRVFDLELHPACRYDALEVFAGSGTSGQRLGRFCGTFRP APLVAPGNQVTLRMTTDEGTGGRGFLLWYSGRATSGTEHQFCGGRLEKAQGTLTTPN WPESDYPPGISCSWHIIAPPDQVIALTFEKFDLEPDTYCRYDSVSVFNGAVSDDSRRLG KFCGDAVPGSISSEGNELLVQFVSDLSVTADGFSASYKTLPRGTAKEGQGPGPKRGTE PKVKLPPKSQPPEKTEESPSAPDAPTCPKQCRRTGTLQSNFCASSLVVTATVKSMVRE PGEGLAVTVSLIGAYKTGGLDLPSPPTGASLKFYVPCKQCPPMKKGVSYLLMGQVEEN BGPVLPPESFVVLHRPNQDQILTNLSKRKCPSQPVRAAASQD

SEQID No:80

MRMTMEEMKNEAETTSMVSMPLYAVMYPVENELERVNLSAAQTLRAAFIKAEKENPGL TQDIIMKILEKKSVEVNFTESLLRMAADDVEEYMIERPEPEFQALNEKARALKQILSKIPD EINDRVRFLQTIKDIASAIKELLDTVNNVFKKYQYQNRRALEHQKKEFVKYSKSFSDTLKT YFKDGKAINVFVSANRLIHQTNLILQTFKTVA

SEQID No:81

MTSALTQGLERIPDQLGYLVLSEGAVLASSGDLENDEQAASAISELVSTACGFRLHRGM NVPFKRLSGEPLPLPLVVVLGAGGYFQGLLGFSSSSLLPSPGVSGLATFLPLGLPGIRIV NEKARERRSSRGHSSSNL

SEQID No:82

MGSRDHLFKVLVVGDAAVGKTSLVQRYSQDSFSKHYKSTVGVDFALKVLQWSDYEIVR LQLWDIAGQERFTSMTRLYYRDASACVIMFDVTNATTFSNSQRWKQDLDSKLTLPNGE PVPCLLLANKCDLSPWAVSRDQIDRFSKENGFTGWTETSVKENKNINEAMRVLIEKMM RNSTEDIMSLSTQGDYINLQTKSSSWSCC

SEQID No:83

MAAAKDTHEDHDTSTENTDESNHDPQFEPIVSLPEQEIKTLEEDEEELFKMRAKLFRFA SENDLPEWKERGTGDVKLLKHKEKGAIRLLMRRDKTLKICANHYITPMMELKPNAGSDR AWVWNTHADFADECPKPELLAIRFLNAENAQKFKTKFEECRKEIEEREKKAGSGKNDH AEKVAEKLEALSVKEETKEDAEEKQ

SEQID No:84

MLDSSDSSSQPHWSNELIAEQLQQQVSQLQDQLDAELEDKRKVLLELSREKAQNEDLK LEVTNILQKHKQEVELLQNAATISQPPDRQSEPATHPAVLQENTQIEPSEPKNQEEKKLS QVLNELQVSHAETTLELEKTRDMLILQRKINVCYQEELEAMMTKADNDNRDHKEKLERL TRLLDLKNNRIKQLEGILRSHDLPTSEQLKDVAYGTRPLSLCLETLPAHGDEDKVDISLLH

QGENLFELHIHQAFLTSAALAQAGDTQPTTFCTYSFYDFETHCTPLSVGPQPLYDFTSQ
YVMETDSLFLHYLQEASARLDIHQAMASEHSTLAAGWICFDRVLETVEKVHGLATLIGA
GGEEFGVLEYWMRLRFPIKPSLQACNKRKKAQVYLSTDVLGGRKAQEEEFRSESWEP
QNELWIEITKCCGLRSRWLGTQPSPYAVYRFFTFSDHDTAIIPASNNPYFRDQARFPVLV
TSDLDHYLRREALSIHVFDDEDLEPGSYLGRARVPLLPLAKNESIKGDFNLTDPAEKPNG
SIQVQLDWKFPYIPPESFLKPEAQTKGKDTKDSSKISSEEEKASFPSQDQMASPEVPIEA
GQYRSKRKPPHGGERKEKEHQVVSYSRRKHGKRIGVQGKNRMEYLSLNILNGNTPQQ
VNYTEWKFSETNSFIGDGFKNQHEEEEMTLSHSALKQKEPLHPVNDKESSEQGSEVSE
AQTTDSDDVIVPPMSQKYPKADSEKMCIEIVSLAFYPEAEVMSDENIKQVYVEYKFYDLP
LSETETPVSLRKPRAGEEIHFHFSKVIDLDPQEQQGRRRFLFDMLNGQDPDQGHLKFTV
VSDPLDEEKKECEEVGYAYLQLWQILESGRDILEQELDIVSPEDLATPIGRLKVSLQAAA
VLHAIYKEMTEDLFS

SEQID No:85

MERSGWARQTFLLALLLGATLRARAAAGYYPRFSPFFFLCTHHGELEGDGEQGEVLISL HIAGNPTYYVPGQEYHVTISTSTFFDGLLVTGLYTSTSVQASQSIGGSSAFGFGIMSDHQ FGNQFMCSVVASHVSHLPTTNLSFIWIAPPAGTGCVNFMATATHRGQVIFKDALAQQLC EQGAPTDVTVHPHLAEIHSDSIILRDDFDSYHQLQLNPNIWVECNNCETGEQCGAIMHG NAVTFCEPYGPRELITTGLNTTTASVLQFSIGSGSCRFSYSDPSIIVLYAKNNSADWIQLE KIRAPSNVSTIIHILYLPEDAKGENVQFQWKQENLRVGEVYEACWALDNILIINSAHRQVV LEDSLDPVDTGNWLFFPGATVKHSCQSDGNSIYFHGNEGSEFNFATTRDVDLSTEDIQ **EQWSEEFESQPTGWDVLGAVIGTECGTIESGLSMVFLKDGERKLCTPSMDTTGYGNLR** FYFVMGGICDPGNSHENDIILYAKIEGRKEHITLDTLSYSSYKVPSLVSVVINPELQTPATK FCLRQKNHQGHNRNVWAVDFFHVLPVLPSTMSHMIQFSINLGCGTHQPGNSVSLEFST NHGRSWSLLHTECLPEICAGPHLPHSTVYSSENYSGWNRITIPLPNAALTRNTRIRWRQ TGPILGNMWAIDNVYIGPSCLKFCSGRGQCTRHGCKCDPGFSGPACEMASQTFPMFIS **ESFGSSRLSSYHNFYSIRGAEVSFGCGVLASGKALVFNKEGRRQLITSFLDSSQSRFLQ** FTLRLGSKSVLSTCRAPDQPGEGVLLHYSYDNGITWKLLEHYSYLSYHEPRIISVELPGD AKQFGIQFRWWQPYHSSQREDVWAIDEIIMTSVLFNSISLDFTNLVEVTQSLGFYLGNV **QPYCGHDWTLCFTGDSKLASSMRYVETQSMQIGASYMIQFSLVMGCGQKYTPHMDN** QVKLEYSTNHGLTWHLVQEECLPSMPSCQEFTSASIYHASEFTQWRRVIVLLPQKTWS SATRFRWSQSYYTAQDEWALDSIYIGQQCPNMCSGHGSCDHGICRCDQGYQGTECH PEAALPSTIMSDFENQNGWESDWQEVIGGEIVKPEQGCGVISSGSSLYFSKAGKRQLV SWDLDTSWVDFVQFYIQIGGESASCNKPDSREEGVLLQYSNNGGIQWHLLAEMYFSDF

SKPRFVYLELPAAAKTPCTRFRWWQPVFSGEDYDQWAVDDIIILSEKQKQIIPVINPTLP QNFYEKPAFDYPMNQMSVWLMLANEGMVKNETFCAATPSAMIFGKSDGDRFAVTRDL TLKPGYVLQFKLNIGCANQFSSTAPVLLQYSHDAGMSWFLVKEGCYPASAGKGCEGNS RELSEPTMYHTGDFEEWTRITIVIPRSLASSKTRFRWIQESSSQKNVPPFGLDGVYISEP CPSYCSGHGDCISGVCFCDLGYTAAQGTCVSNVPNHNEMFDRFEGKLSPLWYKITGA QVGTGCGTLNDGKSLYFNGPGKREARTVPLDTRNIRLVQFYIQIGSKTSGITCIKPRTRN **EGLIVQYSNDNGILWHLLRELDFMSFLEPQIISIDLPQDAKTPATAFRWWQPQHGKHSA** QWALDDVLIGMNDSSQTGFQDKFDGSIDLQANWYRIQGGQVDIDCLSMDTALIFTENIG KPRYAETWDFHVSASTFLQFEMSMGCSKPFSNSHSVQLQYSLNNGKDWHLVTEECVP PTIGCLHYTESSIYTSERFQNWKRITVYLPLSTISPRTRFRWIQANYTVGADSWAIDNVVL ASGCPWMCSGRGICDAGRCVCDRGFGGPYCVPVVPLPSILKDDFNGNLHPDLWPEVY GAERGNLNGETIKSGTSLIFKGEGLRMLISRDLDCTNTMYVQFSLRFIAKSTPERSHSILL QFSISGGITWHLMDEFYFPQTTNILFINVPLPYTAQTNATRFRLWQPYNNGKKEEIWIVD DFIIDGNNVNNPVMLLDTFDFGPREDNWFFYPGGNIGLYCPYSSKGAPEEDSAMVFVS NEVGEHSITTRDLNVNENTIIQFEINVGCSTDSSSADPVRLEFSRDFGATWHLLLPLCYH SSSHVSSLCSTEHHPSSTYYAGTMQGWRREVVHFGKLHLCGSVRFRWYQGFYPAGS QPVTWAIDNVYIGPQCEEMCNGQGSCINGTKCICDPGYSGPTCKISTKNPDFLKDDFEG QLESDRFLLMSGGKPSRKCGILSSGNNLFFNEDGLRMLMTRDLDLSHARFVQFFMRLG CGKGVPDPRSQPVLLQYSLNGGLSWSLLQEFLFSNSSNVGRYIALEIPLKARSGSTRLR WWQPSENGHFYSPWVIDQILIGGNISGNTVLEDDFTTLDSRKWLLHPGGTKMPVCGST **GDALVFIEKASTRYVVSTDVAVNEDSFLQIDFAASCSVTDSCYAIELEYSVDLGLSWHPL** VRDCLPTNVECSRYHLQRILVSDTFNKWTRITLPLPPYTRSQATRFRWHQPAPFDKQQ TWAIDNYYIGDGCIDMCSGHGRCIQGNCVCDEQWGGLYCDDPETSLPTQLKDNFNRA PSSQNWLTVNGGKLSTVCGAVASGMALHFSGGCSRLLVTVDLNLTNAEFIQFYFMYGC LITPNNRNQGVLLEYSVNGGITWNLLMEIFYDQYSKPGFVNILLPPDAKEIATRFRWWQP RHDGLDQNDWAIDNVLISGSADQRTVMLDTFSSAPVPQHERSPADAGPVGRIAFDMFM **EDKTSVNEHWLFHDDCTVERFCDSPDGVMLCGSHDGREVYAVTHDLTPTEGWIMQFK** ISVGCKVSEKIAQNQIHVQYSTDFGVSWNYLVPQCLPADPKCSGSVSQPSVFFPTKGW KRITYPLPESLVGNPVRFRFYQKYSDMQWAIDNFYLGPGCLDNCRGHGDCLREQCICD PGYSGPNCYLTHTLKTFLKERFDSEEIKPDLWMSLEGGSTCTECGILAEDTALYFGGST VRQAVTQDLDLRGAKFLQYWGRIGSENNMTSCHRPICRKEGVLLDYSTDGGITWTLLH **EMDYQKYISVRHDYILLPEDALTNTTRLRWWQPFVISNGIVVSGVERAQWALDNILIGGA** EINPSQLVDTFDDEGTSHEENWSFYPNAVRTAGFCGNPSFHLYWPNKKKDKTHNALSS RELIIQPGYMMQFKIVVGCEATSCGDLHSVMLEYTKDARSDSWQLVQTQCLPSSSNSIG CSPFQFHEATIYNSVNSSSWKRITIQLPDHVSSSATQFRWIQKGEETEKQSWAIDHVYIG EACPKLCSGHGYCTTGAICICDESFQGDDCSVFSHDLPSYIKDNFESARVTEANWETIQ GGVIGSGCGQLAPYAHGDSLYFNGCQIRQAATKPLDLTRASKIMFVLQIGSMSQTDSCN SDLSGPHAVDKAVLLQYSVNNGITWHVIAQHQPKDFTQAQRVSYNVPLEARMKGVLLR WWQPRHNGTGHDQWALDHVEVVLVSTRKQNYMMNFSRQHGLRHFYNRRRSLRRY P

SEQID No:86

MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQL ERIEEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVA SQPARVVDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDT QNRQIDRIMEKADSNKTRIDEANQRATKMLGSG

SEQID No:87

MASTISAYKEKMKELSVLSLICSCFYTQPHPNTVYQYGDMEVKQLDKRASGQSFEVILK SPSDLSPESPMLSSPPKKKDTSLEELQKRLEAAEERRKTQEAQVLKQLAERREHEREV LHKALEENNNFSRQAEEKLNYKMELSKEIREAHLAALRERLREKELHAAEVRRNKEQRE EMSG

SEQID No:88

MKDRTQELRTAKDSDDDDDDVAVTVDRDRFMDEFFEQVEEIRGFIDKIAENVEEVKRKHS AILASPNPDEKTKEELEELMSDIKKTANKVRSKLKSIEQSIEQEEGLNRSSADLRIRKTQH STLSRKFVEVMSEYNATQSDYRERCKGRIQRQLEITGRTTTSEELEDMLESGNPAIFAS GIIMDSSISKQALSEIETRHSEIIKLENSIRELHDMFMDMAMLVESQGEMIDRIEYNVEHAV DYVERAVSDTKKAVKYQSKARRKKIMIIICCVILGIVIASTVGGIFA

SEQID No:89

MAASMFYGRLVAVATLRNHRPRTAQRAAAQVLGSSGLFNNHGLQVQQQQQRNLSLHE YMSMELLQEAGVSVPKGYVAKSPDEAYAIAKKLGSKDVVIKAQVLAGGRGKGTFESGL KGGVKIVFSPEEAKAVSSQMIGKKLFTKQTGEKGRICNQVLVCERKYPRREYYFAITME RSFQGPVLIGSSHGGVNIEDVAAETPEAIIKEPIDIEEGIKKEQALQLAQKMGFPPNIVESA AENMVKLYSLFLKYDATMIEINPMVEDSDGAVLCMDAKINFDSNSAYRQKKIFDLQDWT QEDERDKDAAKANLNYIGLDGNIGCLVNGAGLAMATMDIIKLHGGTPANFLDVGGGATV

HQVTEAFKLITSDKKVLAILVNIFGGIMRCDVIAQGIVMAVKDLEIKIPVVVRLQGTRVDDA KALIADSGLKILACDDLDEAARMVVKLSEIVTLAKQAHVDVKFQLPI

SEQID No:90

MAPLDLDKYVEIARLCKYLPENDLKRLCDYVCDLLLEESNVQPVSTPVTVCGDIHGQFY
DLCELFRTGGQVPDTNYIFMGDFVDRGYYSLETFTYLLALKAKWPDRITLLRGNHESRQ
ITQVYGFYDECQTKYGNANAWRYCTKVFDMLTVAALIDEQILCVHGGLSPDIKTLDQIRTI
-ERNQEIPHKGAFCDLVWSDPEDVDTWAISPRGAGWLFGAKVTNEFVHINNLKLICRAH
QLVHEGYKFMFDEKLVTVWSAPNYCYRCGNIASIMVFKDVNTREPKLFRAVPDSERVIP
PRTTTPYFL

SEQID No:91

MATRSSRRESRLPFLFTLVALLPPGALCEVWTQRLHGGSAPLPQDRGFLVVQGDPREL RLWARGDARGASRADEKPLRRKRSAALQPEPIKVYGQVSLNDSHNQMVVHWAGEKS NVIVALARDSLALARPKSSDVYVSYDYGKSFKKISDKLNFGLGNRSEAVIAQFYHSPADN KRYIFADAYAQYLWITFDFCNTLQGFSIPFRAADLLLHSKASNLLLGFDRSHPNKQLWKS DDFGQTWIMIQEHVKSFSWGIDPYDKPNTIYIERHEPSGYSTVFRSTDFFQSRENQEVIL **EEVRDFQLRDKYMFATKVVHLLGSEQQSSVQLWVSFGRKPMRAAQFVTRHPINEYYIA** DASEDQVFVCVSHSNNRTNLYISEAEGLKFSLSLENVLYYSPGGAGSDTLVRYFANEPF **ADFHRVEGLQGVYIATLINGSMNEENMRSVITFDKGGTWEFLQAPAFTGYGEKINCELS** QGCSLHLAQRLSQLLNLQLRRMPILSKESAPGLIIATGSVGKNLASKTNVYISSSAGARW REALPGPHYYTWGDHGGIITAIAQGMETNELKYSTNEGETWKTFIFSEKPVFVYGLLTEP GEKSTVFTIFGSNKENVHSWLILQVNATDALGVPCTENDYKLWSPSDERGNECLLGHK TVFKRRTPHATCFNGEDFDRPVVVSNCSCTREDYECDFGFKMSEDLSLEVCVPDPEFS GKSYSPPVPCPVGSTYRRTRGYRKISGDTCSGGDVEARLEGELVPCPLAEENEFILYAV RKSIYRYDLASGATEQLPLTGLRAAVALDFDYEHNCLYWSDLALDVIQRLCLNGSTGQE VIINSGLETVEALAFEPLSQLLYWVDAGFKKIEVANPDGDFRLTIVNSSVLDRPRALVLVP QEGVMFWTDWGDLKPGIYRSNMDGSAAYHLVSEDVKWPNGISVDDQWIYWTDAYLE CIERITFSGQQRSVILDNLPHPYAIAVFKNEIYWDDWSQLSIFRASKYSGSQMEILANQLT GLMDMKIFYKGKNTGSNACVPRPCSLLCLPKANNSRSCRCPEDVSSSVLPSGDLMCD CPQGYQLKNNTCVKEENTCLRNQYRCSNGNCINSIWWCDFDNDCGDMSDERNCPTTI CDLDTQFRCQESGTCIPLSYKCDLEDDCGDNSDESHCEMHQCRSDEYNCSSGMCIRS SWVCDGDNDCRDWSDEANCTAIYHTCEASNFQCRNGHCIPQRWACDGDTDCQDGS DEDPVNCEKKCNGFRCPNGTCIPSSKHCDGLRDCSDGSDEQHCEPLCTHFMDFVCKN

RQQCLFHSMVCDGIIQCRDGSDEDAAFAGCSQDPEFHKVCDEFGFQCQNGVCISLIWK CDGMDDCGDYSDEANCENPTEAPNCSRYFQFRCENGHCIPNRWKCDRENDCGDWS DEKDCGDSHILPFSTPGPSTCLPNYYRCSSGTCVMDTWVCDGYRDCADGSDEEACPL LANVTAASTPTQLGRCDRFEFECHQPKTCIPNWKRCDGHQDCQDGRDEANCPTHSTL TCMSREFQCEDGEACIVLSERCDGFLDCSDESDEKACSDELTVYKVQNLQWTADFSG DVTLTWMRPKKMPSASCVYNVYYRVVGESIWKTLETHSNKTNTVLKVLKPDTTYQVKV QVQCLSKAHNTNDFVTLRTPEGLPDAPRNLQLSLPREAEGVIVGHWAPPIHTHGLIREYI VEYSRSGSKMWASQRAASNFTEIKNLLVNTLYTVRVAAVTSRGIGNWSDSKSITTIKGK VIPPPDIHIDSYGENYLSFTLTMESDIKVNGYVVNLFWAFDTHKQERRTLNFRGSILSHKV GNLTAHTSYEISAWAKTDLGDSPLAFEHVMTRGVRPPAPSLKAKAINQTAVECTWTGP RNVVYGIFYATSFLDLYRNPKSLTTSLHNKTVIVSKDEQYLFLVRVVVPYQGPSSDYVVV KMIPDSRLPPRHLHVVHTGKTSVVIKWESPYDSPDQDLLYAIAVKDLIRKTDRSYKVKSR NSTVEYTLNKLEPGGKYHIIVQLGNMSKDSSIKITTVSLSAPDALKIITENDHVLLFWKSLA LKEKHFNESRGYEIHMFDSAMNITAYLGNTTDNFFKISNLKMGHNYTFTVQARCLFGNQI CGEPAILLYDELGSGADASATQAARSTDVAAVVVPILFLILLSLGVGFAILYTKHRRLQSS FTAFANSHYSSRLGSAIFSSGDDLGEDDEDAPMITGFSDDVPMVIA

SEQID No:92

MEGASFGAGRAGAALDPVSFARRPQTLLRVASWVFSIAVFGPIVNEGYVNTDSGPELR CVFNGNAGACRFGVALGLGAFLACAAFLLLDVRFQQISSVRDRRRAVLLDLGFSGLWS FLWFVGFCFLTNQWQRTAPGPATTQAGDAARAAIAFSFFSILSWVALTVKALQRFRLGT DMSLFATEQLSTGASQAYPGYPVGSGVEGTETYQSPPFTETLDTSPKGYQVPAY

SEQID No:93

MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEE VCIHIAHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGM NPREPAVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELST EEEIHHFKNESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTRLR LRNVFRRFLRDFQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPC YIRDSGVAPTDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQ ASLFGKKAKAHKAFGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSL PSRAAALSFVSLVDGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPE DGLYLIHWSTSHPYRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPS VRELGAALQGCLLRAGDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRV

DQKEITQLSHLGQGTRTNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVL KVLDPSHHDIALAFYETASLMSQVSHTHLAFVHGVCVRGPENSMVTEYVEHGPLDVWL RRERGHVPMAWKMVVAQQLASALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKL SDPGVGLGALSREERVERIPWLAPECLPGGANSLSTAMDKWGFGATLLEICFDGEAPL QSRSPSEKEHFYQRQHRLPEPSCPQLATLTSQCLTYEPTQRPSFRTILRDLTRVQPHNL ADVLTVNRDSPAVGPTTFHKRYLKKIRDLGEGHFGKVSLYCYDPTNDGTGEMVAVKAL KADCGPQHRSGWKQEIDILRTLYHEHIIKYKGCCEDQGEKSLQLVMEYVPLGSLRDYLP RHSIGLAQLLLFAQQICEGMAYLHAHDYIHRDLAARNVLLDNDRLVKIGDFGLAKAVPEG HEYYRVREDGDSPVFWYAPECLKEYKFYYASDVWSFGVTLYELLTHCDSSQSPPTKFL ELIGIAQGQMTVLRLTELLERGERLPRPDKCPCEVYHLMKNCWETEASFRPTFENLIPIL KTVHEKYQGQAPSVFSVC

SEQID No:94

MVLIWRRSRYLLREIEAQWSISALWEGFQKWRDNLFLQIVQLIQHVYSVWTASRTVFIKII
VTRHTSTGGGFCDCGDTEAWKTGPFCVNHEPGRAGTIKENSRCPLNEEVIVQARKIFP
SVIKYVVEMTIWEEEKELPPELQIREKNERYYCVLFNDEHHSYDHVIYSLQRALDCELAE
AQLHTTAIDKEGRRAVKAGAYAACQEAKEDIKSHSENVSQHPLHVEVLHSEIMAHQKFA
LRLGSWMNKIMSYSSDFRQIFCQACLREEPDSENPCLISRLMLWDAKLYKGARKILHELI
FSSFFMEMEYKKLFAMEFVKYYKQLQKEYISDDHDRSISITALSVQMFTVPTLARHLIEE
QNVISVITETLLEVLPEYLDRNNKFNFQGYSQDKLGRVYAVICDLKYILISKPTIWTERLR
MQFLEGFRSFLKILTCMQGMEEIRRQVGQHIEVDPDWEAAIAIQMQLKNILLMFQEWCA
CDEELLLVAYKECHKAVMRCSTSFISSSKTVVQSCGHSLETKSYRVSEDLVSIHLPLSRT
LAGLHVRLSRLGAVSRLHEFVSFEDFQVEVLVEYPLRCLVLVAQVVAEMWRRNGLSLIS
QVFYYQDVKCREEMYDKDIIMLQIGASLMDPNKFLLLVLQRYELAEAFNKTISTKDQDLIK
QYNTLIEEMLQVLIYIVGERYVPGVGNVTKEEVTMREIIHLLCIEPMPHSAIAKNLPEN

SEQID No:95

MKALRLSASALFCLLLINGLGAAPPGRPEAQPPPLSSEHKEPVAGDAVPGPKDGSAPEV RGARNSEPQDEGELFQGVDPRALAAVLLQALDRPASPPAPSGSQQGPEEEAAEALLTE TVRSQTHSLPAAGEPEPAAPPRPQTPENGPEASDPSEELEALASLLQELRDFSPSSAK RQQETAAAETETRTHTLTRVNLESPGPERVWRASWGEFQARVPERAPLPPPAPSQFQ ARMPDSGPLPETHKFGEGVSSPKTHLGEALAPLSKAYQGVAAPFPKARRAESALLGGS EAGERLLQQGLAQVEAGRRQAEATRQAAAQEERLADLASDLLLQYLLQGGARQRGLG GRGLQEAAEERESAREEEEAEQERRGGEERVGEEDEEAAEAAEAEADEAERARQNAL

LFAEEEDGEAGAEDKRSQEETPGHRRKEAEGTEEGGEEEDDEEMDPQTIDSLIELSTK LHLPADDVVSIIEEVEEKRNRKKKAPPEPVPPRAAPAPTHVRSPQPPPPPPSARDELP DWNEVLPPWDREEDEVYPPGPYHPFPNYIRPRTLQPPSALRRRHYHHALPPSRHYPG REAQARHAQQEEAEAEERRLQEQEELENYIEHVLLRRP

SEQID No:96

MAHRKLESVGSGMLDHRVRPGPVPHSQEPESEDMELPLEGYVPEGLELAALRPESPA
PEEQECHNHSPDGDSSSDYVNNTSEEEDYDEGLPEEEEGITYYIRYCPEDDSYLEGMD
CNGEEYLAHSAHPVDTDECQEAVEEWTDSAGPHPHGHEAEGSQDYPDGQLPIPEDEP
SVLEAHDQEEDGHYCASKEGYQDYYPEEANGNTGASPYRLRRGDGDLEDQEEDIDQI
VAEIKMSLSMTSITSASEASPEHGPEPGPEDSVEACPPIKASCSPSRHEARPKSLNLLPE
AKHPGDPQRGFKPKTRTPEERLKWPHEQVCNGLEQPRKQQRSDLNGPVDNNNIPETK
KVASFPSFVAVPGPCEPEDLIDGIIFAANYLGSTQLLSERNPSKNIRMMQAQEAVSRVKR
MQKAAKIKKKANSEGDAQTLTEVDLFISTQRIKVLNADTQETMMDHALRTISYIADIGNIV
VLMARRRMPRSASQDCIETTPGAQEGKKQYKMICHVFESEDAQLIAQSIGQAFSVAYQ
EFLRANGINPEDLSQKEYSDIINTQEMYNDDLIHFSNSENCKELQLEKHKGEILGVVVVE
SGWGSILPTVILANMMNGGPAARSGKLSIGDQIMSINGTSLVGLPLATCQGIIKGLKNQT
QVKLNIVSCPPVTTVLIKRPDLKYQLGFSVQNGIICSLMRGGIAERGGVRVGHRIIEINGQ
SVVATAHEKIVQALSNSVGEIHMKTMPAAMFRLLTGQETPLYI

SEQID No:97

MDTSSVGGLELTDQTPVLLGSTAMATSLTNVGNSFSGPANPLVSRSNKFQNSSVEDDD DVVFIEPVQPPPPSVPVVADQRTITFTSSKNEELQGNDSKITPSSKELASQKGSVSETIVI DDEEDMETNQGQEKNSSNFIERRPPETKNRTNDVDFSTSSFSRSKVNAGMGNSGITTE PDSEIQIANVTTLETGVSSVNDGQLENTDGRDMNLMITHVTSLQNTNLGDVSNGLQSSN FGVNIQTYTPSLTSQTKTGVGPFNPGRMNVAGDVFQNGESATHHNPDSWISQSASFPR NQKQPGVDSLSPVASLPKQIFQPSVQQQPTKPVKVTCANCKKPLQKGQTAYQRKGSA HLFCSTTCLSSFSHKPAPKKLCVMCKKDITTMKGTIVAQVDSSESFQEFCSTSCLSLYED KQNPTKGALNKSRCTICGKLTEIRHEVSFKNMTHKLCSDHCFNRYRMANGLIMNCCEQ CGEYLPSKGAGNNVLVIDGQQKRFCCQSCVSEYKQVGSHPSFLKEVRDHMQDSFLMQ PEKYGKLTTCTGCRTQCRFFDMTQCIGPNGYMEPYCSTACMNSHKTKYAKSQSLGIIC HFCKRNSLPQYQATMPDGKLYNFCNSSCVAKFQALSMQSSPNGQFVAPSDIQLKCNY CKNSFCSKPEILEWENKVHQFCSKTCSDDYKKLHCIVTYCEYCQEEKTLHETVNFSGVK RPFCSEGCKLLYKQDFARRLGLRCVTCNYCSQLCKKGATKELDGVVRDFCSEDCCKKF

QDWYYKAARCDCCKSQGTLKERVQWRGEMKHFCDQHCLLRFYCQQNEPNMTTQKG
PENLHYDQGCQTSRTKMTGSAPPPSPTPNKEMKNKAVLCKPLTMTKATYCKPHMQTK
SCQTDDTWRTEYVPVPIPVPVYIPVPMHMYSQNIPVPTTVPVPVPVPVPVPVPLPAPLDSSEKI
PAAIEELKSKVSSDALDTELLTMTDMMSEDEGKTETTNINSVIIETDIIGSDLLKNSDPETQ
SSMPDVPYEPDLDIEIDFPRAAEELDMENEFLLPPVFGEEYEEQPRPRSKKKGAKRKAV
SGYQSHDDSSDNSECSFPFKYTYGVNAWKHWVKTRQLDEDLLVLDELKSSKSVKLKE
DLLSHTTAELNYGLAHFVNEIRRPNGENYAPDSIYYLCLGIQEYLCGSNRKDNIFIDPGY
QTFEQELNKILRSWQPSILPDGSIFSRVEEDYLWRIKQLGSHSPVALLNTLEYFNTKYFG
LKTVEQHLRLSFGTVFRHWKKNPLTMENKACLRYQVSSLCGTDNEDKITTGKRKHEDD
EPVFEQIENTANPSRCPVKMFECYLSKSPQNLNQRMDVFYLQPECSSSTDSPVWYTST
SLDRNTLENMLVRVLLVKDIYDKDNYELDEDTD

SEQID No:98

MARHVFLTGPPGVGKTTLIHKASEVLKSSGVPVDGFYTEEVRQGGRRIGFDVVTLSGTR GPLSRVGLEPPPGKRECRVGQYVVDLTSFEQLALPVLRNADCSSGPGQRVCVIDEIGK MELFSQLFIQAVRQTLSTPGTIILGTIPVPKGKPLALVEEIRNRKDVKVFNVTKENRNHLL PDIVTCVQSSRK

SEQID No:99

MAAPPEPGEPEERKSLKLLGFLDVENTPCARHSILYGSLGSVVAGFGHFLFTSRIRRSC DVGVGGFILVTLGCWFHCRYNYAKQRIQERIAREEIKKKILYEGTHLDPERKHNGSSSN

SEQID No:100

MLSLDFLDDVRRMNKRQLYYQVLNFGMIVSSALMIWKGLMVITGSESPIVVVLSGSMEP AFHRGDLLFLTNRVEDPIRVGEIVVFRIEGREIPIVHRVLKIHEKQNGHIKFLTKGDNNAVD DRGLYKQGQHWLEKKDVVGRARGFVPYIGIVTILMNDYPKFKYAVLFLLGLFVLVHRE

SEQID

No:101AESDLQLAQIKCNLGRAVQLQELWPGGLFWTRKLSTYIRLYGRKFSKEDHVLFIK LLYELVSIPKLEISMMQGFARLLINLLKKKELLSRADLELPWRPLYDMVERILYSKTEHLG LNWFPNSVENILKTLVKSCRPYFPADATAEMLEEWRPLMCPFDVTMQKAITYFEIFLPTS LPPELHHKGFKLWFDELIGLWVSVQNLPQWEGQLVNLFARLATDNIGYIDWDPYVPKIF TRILRSLNLPVGSSQVLVPRFLTNAYDIGHAVIWITAMMGGPSKLVQKHLAGLFNSITSFY HPSNNGRWLNKLMKLLQRLPNSVVRRLHRERYKKPSWLTPVPDSHKLTDQDVTDFVQ

CIIQPVLLAMFSKTGSLEAAQALQNLALMRPELVIPPVLERTYPALETLTEPHQLTATLSC VIGVARSLVSGGRWFPEGPTHMLPLLMRALPGVDPNDFSKCMITFQFIATFSTLVPLVD CSSVLQERNDLTEVERELCSATAEFEDFVLQFMDRCFGLIESSTLEQTREETETEKMTH LESLVELGLSSTFSTILTQCSKEIFMVALQKVFNFSTSHIFETRVAGRMVADMCRAAVKC CPEESLKLFVPHCCSVITQLTMNDDVLNDEELDKELLWNLQLLSEITRVDGRKLLLYREQ LVKILQRTLHLTCKQGYTLSCNLLHHLLRSTTLIYPTEYCSVPGGFDKPPSEYFPIKDWG KPGDLWNLGIQWHVPSSEEVSFAFYLLDSFLQPELVKLQHCGDGKLEMSRDDILQSLTI VHNCLIGSGNLLPPLKGEPVTNLVPSMVSLEETKLYTGLEYDLSRENHREVIATVIRKLLN HILDNSEDDTKSLFLIIKIIGDLLQFQGSHKHEFDSRWKSFNLVKKSMENRLHGKKQHIRA LLIDRVMLQHELRTLTVEGCEYKKIHQDMIRDLLRLSTSSYSQVRNKAQQTFFAALGAYN **FCCRDIIPLVLEFLRPDRQGVTQQQFKGALYCLLGNHSGVCLANLHDWDCIVQTWPAIV** SSGLSQAMSLEKPSIVRLFDDLAEKIHRQYETIGLDFTIPKSCVEIAELLQQSKNPSINQIL LSPEKIKEGIKRQQEKNADALRNYENLVDTLLDGVEQRNLPWKFEHIGIGLLSLLLRDDR VLPLRAIRFFVENLNHDAIVVRKMAISAVAGILKQLKRTHKKLTINPCEISGCPKPTQIIAGD RPDNHWLHYDSKTIPRTKKEWESSCFVEKTHWGYYTWPKNMVVYAGVEEQPKLGRS REDMTEAEQIIFDHFSDPKFVEQLITFLSLEDRKGKDKFNPRRFCLFKGIFRNFDDAFLPV LKPHLEHLVADSHESTQRCVAEIIAGLIRGSKHWTFEKVEKLWELLCPLLRTALSNITVET YNDWGACIATSCESRDPRKLHWLFELLLESPLSGEGGSFVDACRLYVLQGGLAQQEW RVPELLHRLLKYLEPKLTQVYKNVRERIGSVLTYIFMIDVSLPNTTPTISPHVPEFTARILE KLKPLMDVDEEIQNHVMEENGIGEEDERTQGIKLLKTILKWLMASAGRSFSTAVTEQLQL LPLFFKIAPVENDNSYDELKRDAKLCLSLMSQGLLYPHQVPLVLQVLKQTARSSSWHAR YTVLTYLQTMVFYNLFIFLNNEDAVKDIRWLVISLLEDEQLEVREMAATTLSGLLQCNFLT MDSPMQIHFEQLCKTKLPKKRKRDPGSVGDTIPSAELVKRHAGVLGLGACVLSSPYDV PTWMPQLLMNLSAHLNDPQPIEMTVKKTLSNFRRTHHDNWQEHKQQFTDDQLLVLTDL LVSPCYYA

SEQID No:102

MSDSVILRSIKKFGEENDGFESDKSYNNDKKSRLQDEKKGDGVRVGFFQLFRFSSSTDI WLMFVGSLCAFLHGIAQPGVLLIFGTMTDVFIDYDVELQELQIPGKACVNNTIVWTNSSL NQNMTNGTRCGLLNIESEMIKFASYYAGIAVAVLITGYIQICFWVIAAARQIQKMRKFYFR RIMRMEIGWFDCNSVGELNTRFSDDINKINDAIADQMALFIQRMTSTICGFLLGFFRGWK LTLVIISVSPLIGIGAATIGLSVSKFTDYELKAYAKAGVVADEVISSMRTVAAFGGEKREVE RYEKNLVFAQRWGIRKGIVMGFFTGFVWCLIFLCYAVAFWYGSTLVLDEGEYTPGTLVQ IFLSVIVGALNLGNASPCLEAFATGRAAATSIFETIDRKPIIDCMSEDGYKLDRIKGEIEFHN

VTFHYPSRPEVKILNDLNMVIKPGEMTALVGPSGAGKSTALQLIQRFYDPCEGMVTVDG
HDIRSLNIQWLRDQIGIVEQEPVLFSTTIAENIRYGREDATMEDIVQAAKEANAYNFIMDL
PQQFDTLVGEGGGQMSGGQKQRVAIARALIRNPKILLLDMATSALDNESEAMVQEVLS
KIQHGHTIISVAHRLSTVRAADTIIGFEHGTAVERGTHEELLERKGVYFTLVTLQSQGNQA
LNEEDIKDATEDDMLARTFSRGSYQDSLRASIRQRSKSQLSYLVHEPPLAVVDHKSTYE
EDRKDKDIPVQEEVEPAPVRRILKFSAPEWPYMLVGSVGAAVNGTVTPLYAFLFSQILG
TFSIPDKEEQRSQINGVCLLFVAMGCVSLFTQFLQGYAFAKSGELLTKRLRKFGFRAML
GQDIAWFDDLRNSPGALTTRLATDASQVQGAAGSQIGMIVNSFTNVTVAMIIAFSFSWK
LSLVILCFFPFLALSGATQTRMLTGFASRDKQALEMVGQITNEALSNIRTVAGIGKERRFI
EALETELEKPFKTAIQKANIYGFCFAFAQCIMFIANSASYRYGGYLISNEGLHFSYVFRVIS
AVVLSATALGRAFSYTPSYAKAKISAARFFQLLDRQPPISVYNTAGEKWDNFQGKIDFVD
CKFTYPSRPDSQVLNGLSVSISPGQTLAFVGSSGCGKSTSIQLLERFYDPDQGKVMIDG
HDSKKVNVQFLRSNIGIVSQEPVLFACSIMDNIKYGDNTKEIPMERVIAAAKQAQLHDFV
MSLPEKYETNVGSQGSQLSRGEKQRIAIARAIVRDPKILLLDEATSALDTESEKTVQVAL
DKAREGRTCIVIAHRLSTIQNADIIAVMAQGVVIEKGTHEELMAQKGAYYKLVTTGSPIS

SEQID No:103

MSLVLNDLLICCRQLEHDRATERKKEVEKFKRLIRDPETIKHLDRHSDSKQGKYLNWDA VFRFLQKYIQKETECLRIAKPNVSASTQASRQKKMQEISSLVKYFIKCANRRAPRLKCQE LLNYIMDTVKDSSNGAIYGADCSNILLKDILSVRKYWCEISQQQWLELFSVYFRLYLKPS **QDVHRVLVARIIHAVTKGCCSQTDGLNSKFLDFFSKAIQCARQEKSSSGLNHILAALTIFL** KTLAVNFRIRVCELGDEILPTLLYIWTQHRLNDSLKEVIIELFQLQIYIHHPKGAKTQEKGA YESTKWRSILYNLYDLLVNEISHIGSRGKYSSGFRNIAVKENLIELMADICHQVFNEDTRS LEISQSYTTTQRESSDYSVPCKRKKIELGWEVIKDHLQKSQNDFDLVPWLQIATQLISKY PASLPNCELSPLLMILSQLLPQQRHGERTPYVLRCLTEVALCQDKRSNLESSQKSDLLK LWNKIWCITFRGISSEQIQAENFGLLGAIIQGSLVEVDREFWKLFTGSACRPSCPAVCCL TLALTTSIVPGAVKMGIEQNMCEVNRSFSLKESIMKWLLFYQLEGDLENSTEVPPILHSN FPHLVLEKILVSLTMKNCKAAMNFFQSVPECEHHQKDKEELSFSEVEELFLQTTFDKMD FLTIVRECGIEKHQSSIGFSVHQNLKESLDRCLLGLSEQLLNNYSSEITNSETLVRCSRLL VGVLGCYCYMGVIAEEEAYKSELFQKANSLMQCAGESITLFKNKTNEEFRIGSLRNMMQ LCTRCLSNCTKKSPNKIASGFFLRLLTSKLMNDIADICKSLASFIKKPFDRGEVESMEDDT NGNLMEVEDQSSMNLFNDYPDSSVSDANEPGESQSTIGAINPLAEEYLSKQDLLFLDML KFLCLCVTTAQTNTVSFRAADIRRKLLMLIDSSTLEPTKSLHLHMYLMLLKELPGEEYPLP MEDVLELLKPLSNVCSLYRRDQDVCKTILNHVLHVVKNLGQSNMDSENTRDAQGQFLT

VIGAFWHLTKERKYIFSVRMALVNCLKTLLEADPYSKWAILNVMGKDFPVNEVFTQFLAD NHHQVRMLAAESINRLFQDTKGDSSRLLKALPLKLQQTAFENAYLKAQEGMREMSHSA **ENPETLDEIYNRKSVLLTLIAVVLSCSPICEKQALFALCKSVKENGLEPHLVKKVLEKVSE** TFGYRRLEDFMASHLDYLVLEWLNLQDTEYNLSSFPFILLNYTNIEDFYRSCYKVLIPHLV IRSHFDEVKSIANQIQEDWKSLLTDCFPKILVNILPYFAYEGTRDSGMAQQRETATKVYD MLKSENLLGKQIDHLFISNLPEIVVELLMTLHEPANSSASQSTDLCDFSGDLDPAPNPPH FPSHVIKATFAYISNCHKTKLKSILEILSKSPDSYQKILLAICEQAAETNNVYKKHRILKIYHL FVSLLLKDIKSGLGGAWAFVLRDVIYTLIHYINQRPSCIMDVSLRSFSLCCDLLSQVCQTA VTYCKDALENHLHVIVGTLIPLVYEQVEVQKQVLDLLKYLVIDNKDNENLYITIKLLDPFPD HVVFKDLRITQQKIKYSRGPFSLLEEINHFLSVSVYDALPLTRLEGLKDLRRQLELHKDQ MVDIMRASQDNPQDGIMVKLVVNLLQLSKMAINHTGEKEVLEAVGSCLGEVGPIDFSTIA IQHSKDASYTKALKLFEDKELQWTFIMLTYLNNTLVEDCVKVRSAAVTCLKNILATKTGH SFWEIYKMTTDPMLAYLQPFRTSRKKFLEVPRFDKENPFEGLDDINLWIPLSENHDIWIK TLTCAFLDSGGTKCEILQLLKPMCEVKTDFCQTVLPYLIHDILLQDTNESWRNLLSTHVQ GFFTSCLRHFSQTSRSTTPANLDSESEHFFRCCLDKKSQRTMLAVVDYMRRQKRPSS GTIFNDAFWLDLNYLEVAKVAQSCAAHFTALLYAEIYADKKSMDDQEKRSLAFEEGSQS TTISSLSEKSKEETGISLQDLLLEIYRSIGEPDSLYGCGGGKMLQPITRLRTYEHEAMWG KALVTYDLETAIPSSTRQAGIIQALQNLGLCHILSVYLKGLDYENKDWCPELEELHYQAA WRNMQWDHCTSVSKEVEGTSYHESLYNALQSLRDREFSTFYESLKYARVKEVEEMCK RSLESVYSLYPTLSRLQAIGELESIGELFSRSVTHRQLSEVYIKWQKHSQLLKDSDFSFQ **EPIMALRTVILEILMEKEMDNSQRECIKDILTKHLVELSILARTFKNTQLPERAIFQIKQYNS VSCGVSEWQLEEAQVFWAKKEQSLALSILKQMIKKLDASCAANNPSLKLTYTECLRVCG** NWLAETCLENPAVIMQTYLEKAVEVAGNYDGESSDELRNGKMKAFLSLARFSDTQYQR IENYMKSSEFENKQALLKRAKEEVGLLREHKIQTNRYTVKVQRELELDELALRALKEDRK RFLCKAVENYINCLLSGEEHDMWVFRLCSLWLENSGVSEVNGMMKRDGMKIPTYKFLP LMYQLAARMGTKMMGGLGFHEVLNNLISRISMDHPHHTLFIILALANANRDEFLTKPEVA RRSRITKNVPKQSSQLDEDRTEAANRIICTIRSRRPQMVRSVEALCDAYIILANLDATQW KTQRKGINIPADQPITKLKNLEDVVVPTMEIKVDHTGEYGNLVTIQSFKAEFRLAGGVNLP KIIDCVGSDGKERRQLVKGRDDLRQDAVMQQVFQMCNTLLQRNTETRKRKLTICTYKV VPLSQRSGVLEWCTGTVPJGEFLVNNEDGAHKRYRPNDFSAFQCQKKMMEVQKKSFE EKYEVFMDVCQNFQPVFRYFCMEKFLDPAIWFEKRLAYTRSVATSSIVGYILGLGDRHV QNILINEQSAELVHIDLGVAFEQGKILPTPETVPFRLTRDIVDGMGITGVEGVFRRCCEKT MEVMRNSQETLLTIVEVLLYDPLFDWTMNPLKALYLQQRPEDETELHPTLNADDQECK

RNLSDIDQSFDKVAERVLMRLQEKLKGVEEGTVLSVGGQVNLLIQQAIDPKNLSRLFPG WKAWV

SEQID No:104

MDLEGDRNGGAKKKNFFKLNNKSEKDKKEKKPTVSVFSMFRYSNWLDKLYMVVGTLA AIIHGAGLPLMMLVFGEMTDIFANAGNLEDLMSNITNRSDINDTGFFMNLEEDMTRYAYY YSGIGAGVLVAAYIQVSFWCLAAGRQIHKIRKQFFHAIMRQEIGWFDVHDVGELNTRLTD DVSKINEGIGDKIGMFFQSMATFFTGFIVGFTRGWKLTLVILAISPVLGLSAAVWAKILSSF TDKELLAYAKAGAVAEEVLAAIRTVIAFGGQKKELERYNKNLEEAKRIGIKKAITANISIGA AFLLIYASYALAFWYGTTLVLSGEYSIGQVLTVFFSVLIGAFSVGQASPSIEAFANARGAA YEIFKIIDNKPSIDSYSKSGHKPDNIKGNLEFRNVHFSYPSRKEVKILKGLNLKVQSGQTV ALVGNSGCGKSTTVQLMQRLYDPTEGMVSVDGQDIRTINVRFLREIIGVVSQEPVLFAT TIAENIRYGRENVTMDEIEKAVKEANAYDFIMKLPHKFDTLVGERGAQLSGGQKQRIAIA RALVRNPKILLLDEATSALDTESEAVVQVALDKARKGRTTIVIAHRLSTVRNADVIAGFDD GVIVEKGNHDELMKEKGIYFKLVTMQTAGNEVELENAADESKSEIDALEMSSNDSRSSLI RKRSTRRSVRGSQAQDRKLSTKEALDESIPPVSFWRIMKLNLTEWPYFVVGVFCAIING GLQPAFAIIFSKIIGVFTRIDDPETKRQNSNLFSLLFLALGIISFITFFLQGFTFGKAGEILTK RLRYMVFRSMLRQDVSWFDDPKNTTGALTTRLANDAAQVKGAIGSRLAVITQNIANLGT GIIISFIYGWQLTLLLLAIVPIIAIAGVVEMKMLSGQALKDKKELEGAGKIATEAIENFRTVVS LTQEQKFEHMYAQSLQVPYRNSLRKAHIFGITFSFTQAMMYFSYAGCFRFGAYLVAHKL MSFEDVLLVFSAVVFGAMAVGQVSSFAPDYAKAKISAAHIIMIIEKTPLIDSYSTEGLMPN TLEGNVTFGEVVFNYPTRPDIPVLQGLSLEVKKGQTLALVGSSGCGKSTVVQLLERFYD PLAGKVLLDGKEIKRLNVQWLRAHLGIVSQEPILFDCSIAENIAYGDNSRVVSQEEIVRAA KEANIHAFIESLPNKYSTKVGDKGTQLSGGQKQRIAIARALVRQPHILLLDEATSALDTES **EKVVQEALDKAREGRTCIVIAHRLSTIQNADLIVVFQNGRVKEHGTHQQLLAQKGIYFSM VSVQAGTKRQ**

SEQID No:105

MFSLSSTVQPQFTVPLSHLINAFHTPKNTSVSLSGVSVSQNQHRDVVPEHEAPSSECM FSDFLTKLNIVSIGKGKIFEGYRSMFMEPAKRMKKSLDTTDNWHIRPEPFSLSIPPSLNLR DLGLSELKIGQIDQLVENLLPGFCKGKNISSHWHTSHVSAQSFFENKYGNLDIFSTLRSS CLYRHHSRALQSICSDLQYWPVFIQSRGFKTLKSRTRRLQSTSERLAETQNIAPSFVKG FLLRDRGSDVESLDKLMKTKNIPEAHQDAFKTGFAEGFLKAQALTQKTNDSLRRTRLILF VLLLFGIYGLLKNPFLSVRFRTTTGLDSAVDPVQMKNVTFEHVKGVEEAKQELQEVVEF

LKNPQKFTILGGKLPKGILLVGPPGTGKTLLARAVAGEADVPFYYASGSEFDEMFVGVG ASRIRNLFREAKANAPCVIFIDELDSVGGKRIESPMHPYSRQTINQLLAEMDGFKPNEGV IIIGATNFPEALDNALIRPGRFDMQVTVPRPDVKGRTEILKWYLNKIKFDQSVDPEIIARGT VGFSGAELENLVNQAALKAAVDGKEMVTMKELEFSKDKILMGPERRSVEIDNKNKTITA YHESGHAIIAYYTKDAMPINKATIMPRGPTLGHVSLLPENDRWNETRAQLLAQMDVSMG GRVAEELIFGTDHITTGASSDFDNATKIAKRMVTKFGMSEKLGVMTYSDTGKLSPETQS AIEQEIRILLRDSYERAKHILKTHAKEHKNLAEALLTYETLDAKEIQIVLEGKKLEVR

SEQID No:106

MDPSMGVNSVTISVEGMTCNSCVWTIEQQIGKVNGVHHIKVSLEEKNATIIYDPKLQTPK TLQEAIDDMGFDAVIHNPDPLPVLTDTLFLTVTASLTLPWDHIQSTLLKTKGVTDIKIYPQK RTVAVTIIPSIVNANQIKELVPELSLDTGTLEKKSGACEDHSMAQAGEVVLKMKVEGMTC **HSCTSTIEGKIGKLQGVQRIKVSLDNQEATIVYQPHLISVEEMKKQIEAMGFPAFVKKQP** KYLKLGAIDVERLKNTPVKSSEGSQQRSPSYTNDSTATFIIDGMHCKSCVSNIESTLSAL QYVSSIVVSLENRSAIVKYNASSVTPESLRKAIEAVSPGLYRVSITSEVESTSNSPSSSSL QKIPLNVVSQPLTQETVINIDGMTCNSCVQSIEGVISKKPGVKSIRVSLANSNGTVEYDPL LTSPETLRGAIEDMGFDATLSDTNEPLVVIAQPSSEMPLLTSTNEFYTKGMTPVQDKEE GKNSSKCYIQVTGMTCASCVANIERNLRREEGIYSILVALMAGKAEVRYNPAVIQPPMIA **EFIRELGFGATVIENADEGDGVLELVVRGMTCASCVHKIESSLTKHRGILYCSVALATNK** AHIKYDPEIIGPRDIIHTIESLGFEASLVKKDRSASHLDHKREIRQWRRSFLVSLFFCIPVM GLMTYMMVMDHHFATLHHNQNMSKEEMINLHSSMFLERQILPGLSVMNLLSFLLCVPV QFFGGWYFYIQAYKALKHKTANMDVLIVLATTIAFAYSLIILLVAMYERAKVNPITFFDTPP MLFVFIALGRWLEHIAKGKTSEALAKLISLQATEATIVTLDSDNILLSEEQVDVELVQRGDII KVVPGGKFPVDGRVIEGHSMVDESLITGEAMPVAKKPGSTVIAGSINQNGSLLICATHVG ADTTLSQIVKLVEEAQTSKAPIQQFADKLSGYFVPFIVFVSIATLLVWIVIGFLNFEIVETYF **PGYNRSISRTETIIRFAFQASITVLCIACPCSLGLATPTAVMVGTGVGAQNGILIKGGEPLE** MAHKVKVVVFDKTGTITHGTPVVNQVKVLTESNRISHHKILAIVGTAESNSEHPLGTAITK YCKQELDTETLGTCIDFQVVPGCGISCKVTNIEGLLHKNNWNIEDNNIKNASLVQIDASN EQSSTSSSMIIDAQISNALNAQQHKVLIGNREWMIRNGLVINNDVNDFMTEHERKGRTA VLVAVDDELCGLIAIADTVKPEAELAIHILKSMGLEVVLMTGDNSKTARSIASQVGITKVFA **EVLPSHKVAKVKQLQEEGKRVAMVGDGINDSPALAMANVGIAIGTGTDVAIEAADVVLIR** NDLLDVVASIDLSRKTVKRIRINFVFALIYNLVGIPIAAGVFMPIGLVLQPWMGSAAMAAS SVSVVLSSLFLKLYRKPTYESYELPARSQIGQKSPSEISVHVGIDDTSRNSPKLGLLDRIV NYSRASINSLLSDKRSLNSVVTSEPDKHSLLVGDFREDDDTAL

SEOID No:107

METPAAAAPAGSLFPSFLLLACGTLVAALLGAAHRLGLFYQLLHKVDKASVRHGGENVA
AVLRAHGVRFIFTLVGGHISPLLVACEKLGIRVVDTRHEVTAVFAADAMARLSGTVGVAA
VTAGPGLTNTVTAVKNAQMAQSPILLLGGAASTLLQNRGALQAVDQLSLFRPLCKFCVS
VRRVRDIVPTLRAAMAAAQSGTPGPVFVELPVDVLYPYFMVQKEMVPAKPPKGLVGRV
VSWYLENYLANLFAGAWEPQPEGPLPLDIPQASPQQVQRCVEILSRAKRPLMVLGSQA
LLTPTSADKLRAAVETLGVPCFLGGMARGLLGRNHPLHIRENRSAALKKADVIVLAGTVC
DFRLSYGRVLSHSSKIIIVNRNREEMLLNSDIFWKPQEAVQGDVGSFVLKLVEGLQGQT
WAPDWVEELREADRQKEQTFREKAAMPVAQHLNPVQVLQLVEETLPDNSILVVDGGD
FVGTAAHLVQPRGPLRWLDPGAFGTLGVGAGFALGAKLCRPDAEVWCLFGDGAFGYS
LIEFDTFVRHKIPVMALVGNDAGWTQISREQVPSLGSNVACGLAYTDYHKAAMGLGAR
GLLLSRENEDQVVKVLHDAQQQCRDGHPVVVNILIGRTDFRDGSIAV

SEQID No:108

MPVLSRPRPWRGNTLKRTAVLLALAAYGAHKVYPLVRQCLAPARGLQAPAGEPTQEAS
GVAAAKAGMNRVFLQRLLWLLRLLFPRVLCRETGLLALHSAALVSRTFLSVYVARLDGR
LARCIARKDPRAFGWQLLQWLLIALPATFVNSAIRYLEGQLALSFRSRLVAHAYRLYFSQ
QTYYRVSNMDGRLRNPDQSLTEDVVAFAASVAHLYSNLTKPLLDVAVTSYTLLRAARSR
GAGTAWPSAIAGLVVFLTANVLRAFSPKFGELVAEEARRKGELRYMHSRVVANSEEIAF
YGGHEVELALLQRSYQDLASQINLILLERLWYVMLEQFLMKYVWSASGLLMVAVPIITAT
GYSESDAEAVKKAALEKKEEELVSERTEAFTIARNLLTAAADAIERIMSSYKEVTELAGYT
ARVHEMFQVFEDVQRCHFKRPRELEDAQAGSGTIGRSGVRVEGPLKIRGQVVDVEQGI
ICENIPIVTPSGEVVVASLNIRVEEGMHLLITGPNGCGKSSLFRILGGLWPTYGGVLYKPP
PQRMFYIPQRPYMSVGSLRDQVIYPDSVEDMQRKGYSEQDLEAILDVVHLHHILQREG
GWEAMCDWKDVLSGGEKQRIGMARMFYHRPKYALLDECTSAVSIDVEGKIFQAAKDA
GIALLSITHRPSLWKYHTHLLQFDGEGGWKFEKLDSAARLSLTEEKQRLEQQLAGIPKM
QRRLQELCQILGEAVAPAHVPAPSPQGPGGLQGAST

SEQID No:109

MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIILVAGAFFWLVSLLLASVVWFILVHVTD RSDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVS GLSFGIISGVFSVINILADALGPGVVGIHGDSPYYFLTSAFLTAAIILLHTFWGVVFFDACE RRRYWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRS LLCRRQEDSRVMVYSALRIPPED

SEQID No:110

MYEGKKTKNMFLTRALEKILADKEVKKAHHSQLRKACEVALEEIKAETEKQSPPHGEAK AGSSTLPPVKSKTNFIEADKYFLPFELACQSKCPRIVSTSLDCLQKLIAYGHLTGNAPDST TPGKKLIDRIIETICGCFQGPQTDEGVQLQIIKALLTAVTSQHIEIHEGTVLQAVRTCYNIYL ASKNLINQTTAKATLTQMLNVIFARMENQALQEAKQMEKERHRQHHHLLPSPVSHHEP ESPQLRYLPPQTVDHISQEHEGDLDLHTNDVDKSLQDDTEPENGSDISSAENEQTEAD QATAAETLSKNEVLYDGENHDCEEKPQDIVQNIVEEMVNIVVGDMGEGTTINASADGNI GTIEDGSDSENIQANGIPGTPISVAYTPSLPDDRLSVSSNDTQESGNSSGPSPGAKFSHI LQKDAFLVFRSLCKLSMKPLSDGPPDPKSHELRSKILSLQLLLSILQNAGPIFRTNEMFIN AIKQYLCVALSKNGVSSVPEVFELSLSIFLTLLSNFKTHLKMQIEVFFKEIFLYILETSTSSF DHKWMVIQTLTRICADAQSVVDIYVNYDCDLNAANIFERLVNDLSKIAQGRGSQELGMS NVQELSLRKKGLECLVSISKCMVEWSKDQYVNPNSQTTLGQEKPSEQEMSEIKHPETIN RYGSLNSLESTSSSGIGSYSTQMSGTDNPEQFEVLKQQKEIIEQGIDLFNKKPKRGIQYL QEQGMLGTTPEDIAQFLHQEERLDSTQVGEFLGDNDKFNKEVMYAYVDQHDFSGKDF VSALRMFLEGFRLPGEAQKIDRLMEKFAARYLECNQGQTLFASADTAYVLAYSIIMLTTD LHSPQVKNKMTKEQYIKMNRGINDSKDLPEEYLSAIYNEIAGKKISMKETKELTIPTKSSK QNVASEKQRRLLYNLEMEQMAKTAKALMEAVSHVQAPFTSATHLEHVRPMFKLAWTP FLAAFSVGLQDCDDTEVASLCLEGIRCAIRIACIFSIQLERDAYVQALARFTLLTVSSGITE MKQKNIDTIKTLITVAHTDGNYLGNSWHEILKCISQLKLAQLIGTGVKPRYISGTVRGREG SLTGTKDQAPDEFVGLGLVGGNVDWKQIASIQESIGETSSQSVVVAVDRIFTGSTRLDG NAIVDFVRWLCAVSMDELLSTTHPRMFSLQKIVEISYYNMGRIRLQWSRIWEVIGDHFNK VGCNPNEDVAIFAVDSLRQLSMKFLEKGELANFRFQKDFLRPFEHIMKRNRSPTIRDMV VRCIAQMVNSQAANIRSGWKNIFSVFHLAASDQDESIVELAFQTTGHIVTLVFEKHFPATI DSFQDAVKCLSEFACNAAFPDTSMEAIRLIRHCAKYVSDRPQAFKEYTSDDMNVAPED RVWVRGWFPILFELSCIINRCKLDVRTRGLTVMFEIMKTYGHTYEKHWWQDLFRIVFRIF DNMKLPEQQTEKAEWMTTTCNHALYAICDVFTQYLEVLSDVLLDDIFAQLYWCVQQDN EQLARSGTNCLENVVILNGEKFTLEIWDKTCNCTLDIFKTTIPHALLTWRPNSGETAPPP PSPVSEKPLDTISQKSVDIHDSIQPRSVDNRPQAPLVSASAVNEEVSKIKSTAKFPEQKL FAALLIKCVVQLELIQTIDNIVFFPATSKKEDAENLAAAQRDAVDFDVRVDTQDQGMYRF LTSQQLFKLLDCLLESHRFAKAFNSNNEQRTALWKAGFKGKSKPNLLKQETSSLACGLR

ILFRMYMDESRVSAWEEVQQRLLNVCSEALSYFLTLTSESHREAWTNLLLLFLTKVLKIS DNRFKAHASFYYPLLCEIMQFDLIPELRAVLRRFFLRIGVVFQISQPPEQELGINKQ

SEQID No:111

MAVSRLDRLFILLDTGTTPVTRKAAAQQLGEVVKLHPHELNNLLSKVLIYLRSANWDTRI AAGQAVEAIVKNVPEWNPVPRTRQEPTSESSMEDSPTTERLNFDRFDICRLLQHGASLL GSAGAEFEVQDEKSGEVDPKERIARQRKLLQKKLGLNMGEAIGMSTEELFNDEDLDYT PTSASFVNKQPTLQAAELIDSEFRAGMSNRQKNKAKRMAKLFAKQRSRDAVETNEKSN DSTDGEPEEKRRKIANVVINQSANDSKVLIDNIPDSSSLIEETNEWPLESFCEELCNDLFN PSWEVRHGAGTGLREILKAHGKSGGKMGDSTLEEMIQQHQEWLEDLVIRLLCVFALDR FGDFVSDEVVAPVRETCAQTLGVVLKHMNETGVHKTVDVLLKLLTQEQWEVRHGGLLG IKYALAVRQDVINTLLPKVLTRIIEGLQDLDDDVRAVAAASLVPVVESLVYLQTQKVPFIIN TLWDALLELDDLTASTNSIMTLLSSLLTYPQVQQCSIQQSLTVLVPRVWPFLHHTISSVR RAALETLFTLLSTQDQNSSSWLIPILPDMLRHIFQFCVLESSQEILDLIHKVWMELLSKAS VQYVVAAACPWMGAWLCLMMQPSHLPIDLNMLLEVKARAKEKTGGKVRQGQSQNKE VLQEYIAGADTIMEDPATRDFVVMRARMMAAKLLGALCCCICDPGVNVVTQEIKPAESL GQLLLFHLNSKSALQRISVALVICEWAALQKECKAVTLAVQPRLLDILSEHLYYDEIAVPF TRMQNECKQLISSLADVHIEVGNRVNNNVLTIDQASDLVTTVFNEATSSFDLNPQVLQQ LDSKRQQVQMTVTETNQEWQVLQLRVHTFAACAVVSLQQLPEKLNPIIKPLMETIKKEE NTLVQNYAAQCIAKLLQQCTTRTPCPNSKIIKNLCSSLCVDPYLTPCVTCPVPTQSGQEN SKGSTSEKDGMHHTVTKHRGIITLYRHQKAAFAITSRRGPTPKAVKAQIADLPAGSSGNI LVELDEAQKPYLVQRRGAEFALTTIVKHFGGEMAVKLPHLWDAMVGPLRNTIDINNFDG KSLLDKGDSPAQELVNSLQVFETAAASMDSELHPLLVQHLPHLYMCLQYPSTAVRHMA **ARCVGVMSKIATMETMNIFLEKVLPWLGAIDDSVKQEGAIEALACVMEQLDVGIVPYIVLL** VVPVLGRMSDQTDSVRFMATQCFATLIRLMPLEAGIPDPPNMSAELIQLKAKERHFLEQ LLDGKKLENYKIPVPINAELRKYQQDGVNWLAFLNKYKLHGILCDDMGLGKTLQSICILA **GDHCHRAQEYARSKLAECMPLPSLVVCPPTLTGHWVDEVGKFCSREYLNPLHYTGPP** TERIRLQHQVKRHNLIVASYDVVRNDIDFFRNIKFNYCILDEGHVIKNGKTKLSKAVKQLT ANYRIILSGTPIQNNVLELWSLFDFLMPGFLGTERQFAARYGKPILASRDARSSSREQEA GVLAMDALHRQVLPFLLRRMKEDVLQDLPPKIIQDYYCTLSPLQVQLYEDFAKSRAKCD **VDETVSSATLSEETEKPKLKATGHVFQALQYLRKLCNHPALVLTPQHPEFKTTAEKLAV** QNSSLHDIQHAPKLSALKQLLLDCGLGNGSTSESGTESVVAQHRILIFCQLKSMLDIVEH DLLKPHLPSVTYLRLDGSIPPGQRHSIVSRFNNDPSIDVLLLTTHVGGLGLNLTGADTVV **FVEHDWNPMRDLQAMDRAHRIGQKRVVNVYRLITRGTLEEKIMGLQKFKMNIANTVISQ** ENSSLQSMGTDQLLDLFTLDKDGKAEKADTSTSGKASMKSILENLSDLWDQEQYDSEY SLENFMHSLK

SEQID No:112

MGGRVFLAFCVWLTLPGAETQDSRGCARWCPQNSSCVNATACRCNPGFSSFSEIITTP
TETCDDINECATPSKVSCGKFSDCWNTEGSYDCVCSPGYEPVSGAKTFKNESENTCQ
DVDECQQNPRLCKSYGTCVNTLGSYTCQCLPGFKFIPEDPKVCTDVNECTSGQNPCH
SSTHCLNNVGSYQCRCRPGWQPIPGSPNGPNNTVCEDVDECSSGQHQCDSSTVCFN
TVGSYSCRCRPGWKPRHGIPNNQKDTVCEDMTFSTWTPPPGVHSQTLSRFFDKVQDL
GRDSKTSSAEVTIQNVIKLVDELMEAPGDVEALAPPVRHLIATQLLSNLEDIMRILAKSLP
KGPFTYISPSNTELTLMIQERGDKNVTMGQSSARMKLNWAVAAGAEDPGPAVAGILSIQ
NMTTLLANASLNLHSKKQAELEEIYESSIRGVQLRRLSAVNSIFLSHNNTKELNSPILFAF
SHLESSDGEAGRDPPAKDVMPGPRQELLCAFWKSDSDRGGHWATEVCQVLGSKNGS
TTCQCSHLSSFTILMAHYDVEDWKLTLITRVGLALSLFCLLLCILTFLLVRPIQGSRTTIHL
HLCICLFVGSTIFLAGIENEGGQVGLRCRLVAGLLHYCFLAAFCWMSLEGLELYFLVVRV
FQGQGLSTRWLCLIGYGVPLLIVGVSAAIYSKGYGRPRYCWLDFEQGFLWSFLGPVTFII
LCNAVIFVTTVWKLTQKFSEINPDMKKLKKARALTITAIAQLFLLGCTWVFGLFIFDDRSLV
LTYVFTILNCLQGAFLYLLHCLLNKKVREEYRKWACLVAGGSKYSEFTSTTSGTGHNQT
RALRASESGI

SEQID No:113

SLQWTAVATFLYAEVFVVLLLCIPFISPKRWQKIFKSRLVELLVSYGNTFFVVLIVILVLLVI DAVREIRKYDDVTEKVNLQNNPGAMEHFHMKLFRAQRNLYIAGFSLLLSFLLRRLVTLIS QQATLLASNEAFKKQAESASEAAKKYMEENDQLKKGAAVDGGKLDVGNAEVKLEEEN RSLKADLQKLKDELASTKQKLEKAENQVLAMRKQSEGLTKEYDRLLEEHAKLQAAVDG PMDKKEE

SEQID No:114

MSFLIDSSIMITSQILFFGFGWLFFMRQLFKDYEIRQYVVQVIFSVTFAFSCTMFELIIFEIL GVLNSSSRYFHWKMNLCVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTFMYFF WKLGDPFPILSPKHGILSIEQLISRVGVIGVTLMALLSGFGAVNCPYTYMSYFLRNVTDTD ILALERRLLQTMDMIISKKKRMAMARRTMFQKGEVHNKPSGFWGMIKSVTTSASGSENL TLIQQEVDALEELSRQLFLETADLYATKERIEYSKTFKGKYFNFLGYFFSIYCVWKIFMATI NIVFDRVGKTDPVTRGIEITVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLITLTKFFYAIS

SSKSSNVIVLLLAQIMGMYFVSSVLLIRMSMPLEYRTIITEVLGELQFNFYHRWFDVIFLVS ALSSILFLYLAHKQAPEKQMAP

SEQID No:115

GEGGESWPPPVFRVRGFVGVALTCSSATADPPSALSSRRSVPPGQLCEAAAGEGTMG
TVHARSLEPLPSSGPDFGGLGEEAEFVEVEPEAKQEILENKDVVVQHVHFDGLGRTKD
DIIICEIGDVFKAKNLIEVMRKSHEAREKLLRLGIFRQVDVLIDTCQGDDALPNGLDVTFEV
TELRRLTGSYNTMVGNNEGSMVLGLKLPNLLGRAEKVTFQFSYGTKETSYGLSFFKPR
PGNFERNFSVNLYKVTGQFPWSSLRETDRGMSAEYSFPIWKTSHTVKWEGVWRELGC
LSRTASFAVRKESGHSLKSSLSHAMVIDSRNSSILPRRGALLKVNQELAGYTGGDVSFIK
EDFELQLNKQLIFDSVFSASFWGGMLVPIGDKPSSIADRFYLGGPTSIRGFSMHSIGPQS
EGDYLGGEAYWAGGLHLYTPLPFRPGQGGFGELFRTHFFLNAGNLCNLNYGEGPKAHI
RKLAECIRWSYGAGIVLRLGNIARLELNYCVPMGVQTGDRICDGVQFGAGIRFL

SEQID No:116

MALAVSLPLALSPPRLLLLLLSLLPVARASEAEHRLFERLFEDYNEIIRPVANVSDPVIIHF
EVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKPDIV
LYNNAVGDFQVDDKTKALLKYTGEVTWIPPAIFKSSCKIDVTYFPFDYQNCTMKFGSWS
YDKAKIDLVLIGSSMNLKDYWESGEWAIIKAPGYKHDIKYNCCEEIYPDITYSLYIRRLPLF
YTINLIIPCLLISFLTVLVFYLPSDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVIPLIGEYLLF
TMIFVTLSIVITVFVLNVHYRTPTTHTMPSWVKTVFLNLLPRVMFMTRPTSNEGNAQKPR
PLYGAELSNLNCFSRAESKGCKEGYPCQDGMCGYCHHRRIKISNFSANLTRSSSSESV
DAVLSLSALSPEIKEAIQSVKYIAENMKAQNEAKEIQDDWKYVAMVIDRIFLWVFTLVCIL
GTAGLFLQPLMAREDA

SEQID No:117

MGSRASTLLRDEELEEIKKETGFSHSQITRLYSRFTSLDKGENGTLSREDFQRIPELAINP LGDRIINAFFPEGEDQVNFRGFMRTLAHFRPIEDNEKSKDVNGPEPLNSRSNKLHFAFR LYDLDKDEKISRDELLQVLRMMVGVNISDEQLGSIADRTIQEADQDGDSAISFTEFVKVL EKVDVEQKMSIRFLH

SEQID No:118

MASESSPLLAYRLLGEEGVALPANGAGGPGGASARKLSTFLGVVVPTVLSMFSIVVFLRI GFVVGHAGLLQALAMLLVAYFILALTVLSVCAIATNGAVQGGGAYFMISRTLGPEVGGSI GLMFYLANVCGCAVSLLGLVESVLDVFGADATGPSGLRVLPQGYGWNLLYGSLLLGLV
GGVCTLGAGLYARASFLTFLLVSGSLASVLISFVAVGPRDIRLTPRPGPNGSSLPPRFGH
FTGFNSSTLKDNLGAGYAEDYTTGAVMNFANVFAVLFNGCTGIMAGANMSGELKDPSR
AIPLGTIVAVAYTFFVYVLLFFLSSFTCDRTLLQEDYGFFRAISLWPPLVLIGIYATALSAS
MSSLIGASRILHALARDDLFGVILAPAKVVSRGGNPWAAVLYSWGLVQLVLLAGKLNTLA
AVVTVFYLVAYAAVDLSCLSLEWASAPNFRPTFSLFSWHTCLLGVASCLLMMFLISPGA
AGGSLLLMGLLAALLTARGGPSSWGYVSQALLFHQVRKYLLRLDVRKDHVKFWRPQLL
LLVGNPRGALPLLRLANQLKKGGLYVLGHVTLGDLDSLPSDPVQPQYGAWLSLVDRAQ
VKAFVDLTFSPSVRQGAQHLLRISGLGGMKPNTLVLGFYDDAPPQDHFLTDPAFSEPAD
STREGSSPALSTLFPPPRAPGSPRALNPQDYVATVADALKMNKNVVLARASGALPPER
LSRGSGGTSQLHHVDVWPLNLLRPRGGPGYVDVCGLFLLQMATILGMVPAWHSARLRI
FLCLGPREAPGAAEGRLRALLSQLRIRAEVQEVVWGEGAGAGEPEAEEEGDFVNSGR
GDAEAEALARSANALVRAQQGRGTGGGPGGPEGGDAEGPITALTFLYLPRPPADPAR
YPRYLALLETLTRDLGPTLLVHGVTPVTCTDL

SEQID No:119

MASFVTEVLAHSGRLEKEDLGTRISRLTRRVEEIKGEVCNMISKKYSEFLPSMQSAQGLI
TQVDKLSEDIDLLKSRIESEVRRDLHVSTGEFTDLKQQLERDSVVLSLLKQLQEFSTAIEE
YNCALTEKKYVTGAQRLEEAQKCLKLLKSRKCFDLKILKSLSMELTIQKQNILYHLGEEW
QKLIVWKFPPSKDTSSLESYLQTELHLYTEQSHKEEKTPMPPISSVLLAFSVLGELHSKL
KSFGQMLLKYILRPLASCPSLHAVIESQPNIVIIRFESIMTNLEYPSPSEVFTKIRLVLEVLQ
KQLLDLPLDTDLENEKTSTVPLAEMLGDMIWEDLSECLIKNCLVYSIPTNSSKLQQYEEII
QSTEEFENALKEMRFLKGDTTDLLKYARNINSHFANKKCQDVIVAARNLMTSEIHNTVKII
PDSKINVPELPTPDEDNKLEVQKVSNTQYHEVMNLEPENTLDQHSFSLPTCRISESVKK
LMELAYQTLLEATTSSDQCAVQLFYSVRNIFHLFHDVVPTYHKENLQKLPQLAAIHHNNC
MYIAHHLLTLGHQFRLRLAPILCDGTATFVDLVPGFRRLGTECFLAQMRAQKGELLERLS
SARNFSNMDDEENYSAASKAVRQVLHQLKRLGIVWQDVLPVNIYCKAMGTLLNTAISEV
IGKITALEDISTEDGDRLYSLCKTVMDEGPQVFAPLSEESKNKKYQEEVPVYVPKWMPF
KELMMMLQASLQEIGDRWADGKGPLAAAFSSSEVKALIRALFQNTERRAAALAKIK

SEQID No:120

MSRLGALGGARAGLGLLLGTAAGLGFLCLLYSQRWKRTQRHGRSQSLPNSLDYTQTS
DPGRHVMLLRAVPGGAGDASVLPSLPREGQEKVLDRLDFVLTSLVALRREVEELRSSL
RGLAGEIVGEVRCHMEENQRVARRRRFPFVRERSDSTGSSSVYFTASSGATFTDAESE

GGYTTANAESDNERDSDKESEDGEDEVSCETVKMGRKDSLDLEEEAASGASSALEAG GSSGLEDVLPLLQQADELHRGDEQGKREGFQLLLNNKLVYGSRQDFLWRLARAYSDM CELTEEVSEKKSYALDGKEEAEAALEKGDESADCHLWYAVLCGQLAEHESIQRRIQSGF SFKEHVDKAIALQPENPMAHFLLGRWCYQVSHLSWLEKKTATALLESPLSATVEDALQS FLKAEELQPGFSKAGRVYISKCYRELGKNSEARWWMKLALELPDVTKEDLAIQKDLEEL EVILRD

SEQID No:121

EIEQNSAMAPRKRGGRGISFIFCCFRNNDHPEITYRLRNDSNFALQTMEPALPMPPVEE LDVMFSELVDELDLTDKHREAMFALPAEKKWQIYCSKKKDQEENKGATSWPEFYIDQL NSMAARKSLLALEKEEEERSKTIESLKTALRTKPMRFVTRFIDLDGLSCILNFLKTMDYE TSESRIHTSLIGCIKALMNNSQGRAHVLAHSESINVIAQSLSTENIKTKVAVLEILGAVCLV PGGHKKVLQAMLHYQKYASERTRFQTLINDLDKSTGRYRDEVSLKTAIMSFINAVLSQG AGVESLDFRLHLRYEFLMLGIQPVIDKLREHENSTLDRHLDFFEMLRNEDELEFAKRFEL VHIDTKSATQMFELTRKRLTHSEAYPHFMSILHHCLQMPYKRSGNTVQYWLLLDRIIQQI VIQNDKGQDPDSTPLENFNIKNVVRMLVNENEVKQWKEQAEKMRKEHNELQQKLEKK **ERECDAKTQEKEEMMQTLNKMKEKLEKETTEHKQVKQQVADLTAQLHELSRRAVCASI** PGGPSPGAPGGPFPSSVPGSLLPPPPPPPLPGGMLPPPPPPLPPGGPPPPPGPPPLG AIMPPPGAPMGLALKKKSIPQPTNALKSFNWSKLPENKLEGTVWTEIDDTKVFKILDLED LERTFSAYQRQQDFFVNSNSKQKEADAIDDTLSSKLKVKELSVIDGRRAQNCNILLSRLK LSNDEIKRAILTMDEQEDLPKDMLEQLLKFVPEKSDIDLLEEHKHELDRMAKADRFLFEM SRINHYQQRLQSLYFKKKFAERVAEVKPKVEAIRSGSEEVFRSGALKQLLEVVLAFGNY MNKGQRGNAYGFKISSLNKIADTKSSIDKNITLLHYLITIVENKYPSVLNLNEELRDIPQAA KVNMTELDKEISTLRSGLKAVETELEYQKSQPPQPGDKFVSVVSQFITVASFSFSDVEDL LAEAKDLFTKAVKHFGEEAGKIQPDEFFGIFDQFLQAVSEAKQENENMRKKKEEEERRA RMEAQLKEQRERERKMRKAKENSEESGEFDDLVSALRSGEVFDKDLSKLKRNRKRITN **QMTDSSRERPITKLNF**

SEQID No:122

MTVFRQENVDDYYDTGEELGSGQFAVVKKCREKSTGLQYAAKFIKKRRTKSSRRGVSR EDIEREVSILKEIQHPNVITLHEVYENKTDVILILELVAGGELFDFLAEKESLTEEEATEFLK QILNGVYYLHSLQIAHFDLKPENIMLLDRNVPKPRIKIIDFGLAHKIDFGNEFKNIFGTPEFV APEIVNYEPLGLEADMWSIGVITYILLSGASPFLGDTKQETLANVSAVNYEFEDEYFSNT SALAKDFIRRLLVKDPKKRMTIQDSLQHPWIKPKDTQQALSRKASAVNMEKFKKFAARK

KWKQSVRLISLCQRLSRSFLSRSNMSVARSDDTLDEEDSFVMKAIIHAINDDNVPGLQH LLGSLSNYDVNQPNKHGTPPLLIAAGCGNIQILQLLIKRGSRIDVQDKGGSNAVYWAARH GHVDTLKFLSENKCPLDVKDKSGEMALHVAARYGHADVAQVTCAASAQIPISRTKEEET PLHCAAWHGYYSVAKALCEAGCNVNIKNREGETPLLTASARGYHDIVECLAEHGADLN **ACDKDGHIALHLAVRRCQMEVIKTLLSQGCFVDYQDRHGNTPLHVACKDGNMPIVVAL** -CEANCNLDISNKYGRTPLHLAANNGILDVVRYLCLMGASVEALTTDGKTAEDLARSEQH EHVAGLLARLRKDTHRGLFIQQLRPTQNLQPRIKLKLFGHSGSGKTTLVESLKCGLLRSF FRRRPRLSSTNSSRFPPSPLASKPTVSVSINNLYPGCENVSVRSRSMMFEPGLTKGM LEVFVAPTHHPHCSADDQSTKAIDIQNAYLNGVGDFSVWEFSGNPVYFCCYDYFAAND PTSIHVVVFSLEEPYEIQLNPVIFWLSFLKSLVPVEEPIAFGGKLKNPLQVVLVATHADIMN **VPRPAGGEFGYDKDTSLLKEIRNRFGNDLHISNKLFVLDAGASGSKDMKVLRNHLQEIR** SQIVSVCPPMTHLCEKIISTLPSWRKLNGPNQLMSLQQFVYDVQDQLNPLASEEDLRRI AQQLHSTGEINIMQSETVQDVLLLDPRWLCTNVLGKLLSVETPRALHHYRGRYTVEDIQ RLVPDSDVEELLQILDAMDICARDLSSGTMVDVPALIKTDNLHRSWADEEDEVMVYGGV RIVPVEHLTPFPCGIFHKVQVNLCRWIHQQSTEGDADIRLWVNGCKLANRGAELLVLLV NHGQGIEVQVRGLETEKIKCCLLLDSVCSTIENVMATTLPGLLTVKHYLSPQQLREHHEP VMIYQPRDFFRAQTLKETSLTNTMGGYKESFSSIMCFGCHDVYSQASLGMDIHASDLNL LTRRKLSRLLDPPDPLGKDWCLLAMNLGLPDLVAKYNTNNGAPKDFLPSPLHALLREW TTYPESTVGTLMSKLRELGRRDAADLLLKASSVFKINLDGNGQEAYASSCNSGTSYNSI **SSVVSR**

SEQID No:123

MWTPTEEKYGVVICSFRGSVPQGLVLEIGETVQILEKCEGWYRGVSTKKPNVKGIFPA
NYIHLKKAIVSNRGQYETVVPLEDSIVTEVTATLQEWASLWKQLYVKHKVDLFYKLRHV
MNELIDLRRQLLSGHLTQDQVREVKRHITVRLDWGNEHLGLDLVPRKDFEVVDSDQISV
SDLYKMHLSSRQSVQQSTSQVDTMRPRHGETCRMPVPHHFFLSLKSFTYNTIGEDTDV
FFSLYDMREGKQISERFLVRLNKNGGPRNPEKIERMCALFTDLSSKDMKRDLYIVAHVIR
IGRMLLNDSKKGPPHLHYRRPYGCAVLSILDVLQSLTEVKEEKDFVLKVYTCNNESEWS
QIHENIIRKSSAKYSAPSASHGLIISLQLLRGDMEQIRRENPMIFNRGLAITRKLGFPDVIM
PGDIRNDLYLTLEKGDFERGGKSVQKNIEVTMYVLYADGEILKDCISLGSGEPNRSSYHS
FVLYHSNSPRWGEIIKLPIPIDRFRGSHLRFEFRHCSTKDKGEKKLFGFAFSTLMRDDGT
TLSDDIHELYVYKCDENSTFNNHALYLGLPCCKEDYNGCPNIPSSLIFQRSTKESFFISTQ
LSSTKLTQNVDLLALLKWKAFPDRIMDVLGRLRHVSGEEIVKFLQDILDTLFVILDDNTEK
YGLLVFQSLVFIINLLRDIKYFHFRPVMDTYIQKHFAGALAYKELIRCLKWYMDCSAELIR

QDHIQEAMRALEYLFKFIVQSRILYSRATCGMEEEQFRSSIQELFQSIRFVLSLDSRNSET LLFTQAALLNSFPTIFDELLQMFTVQEVAEFVRGTLGSMPSTVHIGQSMDVVKLQSIART VDSRLFSFSESRRILLPVVLHHIHLHLRQQKELLICSGILGSIFSIVKTSSLEADVMEEVEM MVESLLDVLLQTLLTIMSKSHAQEAVRGQRCPQCTAEITGEYVSCLLSLLRQMCDTHFQ HLLDNFQSKDELKEFLLKIFCVFRNLMKMSVFPRDWMVMRLLTSNIIVTTVQYLSSALHK NFTETDFDFKVWNSYFSLAVLFINQPSLQLEIITSAKRKKILDKYGDMRVMMAYELFSMW QNLGEHKIHFIPGMIGPFLGVTLVPQPEVRNIMIPIFHDMMDWEQRKNGNFKQVEAELID KLDSMVSEGKGDESYRELFSLLTQLFGPYPSLLEKVEQETWRETGISFVTSVTRLMERL LDYRDCMKGEETENKKIGCTVNLMNFYKSEINKEEMYIRYIHKLCDMHLQAENYTEAAF TLLLYCELLQWEDRPLREFLHYPSQTEWQRKEGLCRKIIHYFNKGKSWEFGIPLCRELA CQYESLYDYQSLSWIRKMEASYYDNIMEQQRLEPEFFRVGFYGRKFPFFLRNKEYVCR GHDYERLEAFQQRMLSEFPQAVAMQHPNHPDDAILQCDAQYLQIYAVTPIPDYVDVLQ MDRVPDRVKSFYRVNNVRKFRYDRPFHKGPKDKENEFKSLWIERTTLTLTHSLPGISR WFEVERRELVEVSPLENAIQVVENKNQELRSLISQYQHKQVHGNINLLSMCLNGVIDAA VNGGIARYQEAFFDKDYINKHPGDAEKITQLKELMQEQVHVLGVGLAVHEKFVHPEMR PLHKKLIDQFQMMRASLYHEFPGLDKLSPACSGTSTPRGNVLASHSPMSPESIKMTHR HSPMNLMGTGRHSSSSLSSHASSEAGNMVMLGDGSMGDAPEDLYHHMQLAYPNPRY QGSVTNVSVLSSSQASPSSSSLSSTHSAPSQMITSAPSSARGSPSLPDKYRHAREMML LLPTYRDRPSSAMYPAAILENGQPPNFQRALFQQVVGACKPCSDPNLSVAEKGHYSLH **FDAFHHPLGDTPPALPARTLRKSPLHPIPASPTSPQSGLDGSNSTLSGSASSGVSSLSE** SNFGHSSEAPPRTDTMDSMPSQAWNADEDLEPPYLPVHYSLSESAVLDSIKAQPCRSH SAPGCVIPQDPMDPPALPPKPYHPRLPALEHDEGVLLREETERPRGLHRKAPLPPGSA KEEQARMAWEHGRGEQ

SEQID No:124

MAATFFGEVVKAPCRAGTEDEEEEEEGRRETPEDREVRLQLARKREVRLLRRQTKTSL EVSLLEKYPCSKFIIAIGNNAVAFLSSFVMNSGVWEEVGCAKLWNEWCRTTDTTHLSST EAFCVFYHLKSNPSVFLCQCSCYVAEDQQYQWLEKVFGSCPRKNMQITILTCRHVTDY KTSESTGSLPSPFLRALKTQNFKDSACCPLLEQPNIVHDLPAAVLSYCQVWKIPAILYLC YTDVMKLDLITVEAFKPILSTRSLKGLVKNIPQSTEILKKLMTTNEIQSNIYT

SEQID No: 125

MSWVQATLLARGLCRAWGGTCGAALTGTSISQVPRRLPRGLHCSAAAHSSEQSLVPS PPEPRORPTKALVPFEDLFGQAPGGERDKASFLQTVQKFAEHSVRKRGHIDFIYLALRK MREYGVERDLAVYNQLLNIFPKEVFRPRNIIQRIFVHYPRQQECGIAVLEQMENHGVMP NKETEFLLIQIFGRKSYPMLKLVRLKLWFPRFMNVNPFPVPRDLPQDPVELAMFGLRHM EPDLSARVTIYQVPLPKDSTGAADPPQPHIVGIQSPDQQAALARHNPARPVFVEGPFSL WLRNKCVYYHILRADLLPPEEREVEETPEEWNLYYPMQLDLEYVRSGWDNYEFDINEV EEGPVFAMCMAGAHDQATMAKWIQGLQETNPTLAQIPVVFRLAGSTRELQTSSAGLEE PPLPEDHQEEDDNLQRQQQGQS

SEQID No:126

MQAHELFRYFRMPELVDFRQCVTLPTNTLMGFGAFSRRLTTFWRPRHPKPLKPPWHL SMQSVEVAGSGGARRSALLDSDEPLVYFYDDVTTLYEGFQRGIQVSNNGPCLGSRKP DQPYEWLSYKQVAELSECIGSALIQKGFKTAPDQFIGIFAQNRPEWVIIEQGCFAYSMVI VPLYDTLGNEAITYIVNKAELSLVFVDKPEKAKLLLEGVENKLIPGLKIIVVMDSYGSELVE RGQRCGVEVTSMKAMEDLGRANRRKPKPPAPEDLAVICFTSGTTGNPKGAMVTHRNIV SDCSAFVKATENTVNPCPDDTLISFLPLAHMFERVVECVMLCHGAKIGFFQGDIRLLMD DLKVLQPTVFPVVPRLLNRMFDRIFGQANTTVKRWLLDFASKRKEADVRSGIIRNNSLW DRLIFHKVQSSLGGRVRLMVTGAAPVSATVLTFLRAALGCQFYEGYGQTECTAGCCLT MPGDWTTGHVGAPMPCNLIKLGWQLEEMNYMASEGEGEVCVKGPNVFQGYLKDPAK TAEALDKDGWLHTGDIGKWLPNGTLKIIDRKKHIFKLAQGEYIAPEKIENIYMRSEPVAQV FVHGESLQAFLIAIVVPDVETLCSWAQKRGFEGSFEELCRNKDVKKAILEDMVRLGKDS GLKPFEQVKGITLHPELFSIDNGLLTPTMKAKRPELRNYFRSQIDDLYSIIKV

SEQID No:127

MPSASCDTLLDDIEDIVSQEDSKPQDRHFVRKDVVPKVRRRNTQKYLQEEENSPPSDS
TIPGIQKIWIRTWGCSHNNSDGEYMAGQLAAYGYKITENASDADLWLLNSCTVKNPAED
HFRNSIKKAQEENKKIVLAGCVPQAQPRQDYLKGLSIIGVQQIDRVVEVVEETIKGHSVR
LLGQKKDNGRRLGGARLDLPKIRKNPLIEIISISTGCLNACTYCKTKHARGNLASYPIDEL
VDRAKQSFQEGVCEIWLTSEDTGAYGRDIGTNLPTLLWKLVEVIPEGAMLRLGMTNPPY
ILEHLEEMAKILNHPRVYAFLHIPVQSASDSVLMEMKREYCVADFKRVVDFLKEKVPGITI
ATDIICGFPGETDQDFQETVKLVEEYKFPSLFINQFYPRPGTPAAKMEQVPAQVKKQRT
KDLSRVFHSYSPYDHKIGERQQVLVTEESFDSKFYVAHNQFYEQVLVPKNPAFMGKMV
EVDIYESGKHFMKGQPVSDAKVYTPSISKPLAKGEVSGLTKDFRNGLGNQLSSGSHTS
AASQCDSASSRMVLPMPRLHQDCALRMSVGLALLGLLFAFFVKVYN

MGGTTSTRRVTFEADENENITVVKGIRLSENVIDRMKESSPSGSKSQRYSGAYGASVS
-DEELKRRVAEELALEQAKKESEDQKRLKQAKELDRERAAANEQLTRAILRERICSEEER
AKAKHLARQLEEKDRVLKKQDAFYKEQLARLEERSSEFYRVTTEQYQKAAEEVEAKFK
RYESHPVCADLQAKILQCYRENTHQTLKCSALATQYMHCVNHAKQSMLEKGG

SEQID No:129

MALAARLLPQFLHSRSLPCGAVRLRTPAVAEVRLPSATLCYFCRCRLGLGAALFPRSAR ALAASALPAQGSRWPVLSSPGLPAAFASFPACPQRSYSTEEKPQQHQKTKMIVLGFSN PINWVRTRIKAFLIWAYFDKEFSITEFSEGAKQAFAHVSKLLSQCKFDLLEELVAKEVLHA LKEKVTSLPDNHKNALAANIDEIVFTSTGDISIYYDEKGRKFVNILMCFWYLTSANIPSETL RGASVFQVKLGNQNVETKQLLSASYEFQREFTQGVKPDWTIARIEHSKLLE

SEQID No:130

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNA
ARRPNSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGI
RQRLLVAVLTSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPI
GHLHLALRHLLEQHGDDFDWFFLVPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFI
GGEPTPGRYCHGGFGVLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCILDATGVG
CTGDHEGVHYSHLELSPGEPVQEGDPHFRSALTAHPVRDPVHMYQLHKAFARAELER
TYQEIQELQWEIQNTSHLAVDGDRAAAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSC
ADGSPRCPLRGADRADVADVLGTALEELNRRYHPALRLQKQQLVNGYRRFDPARGME
YTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEILPVPYVTEASRLTVLLPLAAAERDLA
PGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVAHADVFAPVKAHVAELERRFPGAR
VPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVLTPDFLNRCRMHAISGWQAFF
PMHFQAFHPAVAPPQGPGPPELGRDTGRFDRQAASEACFYNSDYVAARGRLAAASEQ
EEELLESLDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDLYHRCLQSVLEGL
GSRTQLAMLLFEQEQGNST

SEQID No:131

MKLKLKNVFLAYFLVSIAGLLYALVQLGQPCDCLPPLRAAAEQLRQKDLRISQLQAELRR PPPAPAQPPEPEALPTIYVVTPTYARLVQKAELVRLSQTLSLVPRLHWLLVEDAEGPTPL VSGLLAASGLLFTHLVVLTPKAQRLREGEPGWVHPRGVEQRNKALDWLRGRGGAVGG EKDPPPGTQGVVYFADDDNTYSRELSEEMRWTRGVSVWPVGLVGGLRFEGPQVQD

GRVVGFHTAWEPSRPFPVDMAGFAVALPLLLDKPNAQFDSTAPRGHLESSLLSHLVDP KDLEPRAANCTRVLVWHTRTEKPKMKQEEQLQRQGRGSDPAIEV

SEQID No:132

MAAPRAGRGAGWSLRAWRALGGIRWGRRPRLTPDLRALLTSGTSDPRARVTYGTPSL WARLSVGVTEPRACLTSGTPGPRAQLTAVTPDTRTREASENSGTRSRAWLAVALGAG GAVLLLLWGGGRGPPAVLAAVPSPPPASPRSQYNFIADVVEKTAPAVVYIEILDRHPFLG REVPISNGSGFVVAADGLIVTNAHVVADRRRVRVRLLSGDTYEAVVTAVDPVADIATLRI QTKEPLPTLPLGRSADVRQGEFVVAMGSPFALQNTITSGIVSSAQRPARDLGLPQTNVE YIQTDAAIDFGNSGGPLVNLDGEVIGVNTMKVTAGISFAIPSDRLREFLHRGEKKNSSSGI SGSQRRYIGVMMLTLSPSILAELQLREPSFPDVQHGVLIHKVILGSPAHRAGLRPGDVIL AIGEQMVQNAEDVYEAVRTQSQLAVQIRRGRETLTLYVTPEVTE

SEQID No:133

MTQLFLWEYGDLHLFGPNQRPAPCYDPCEAVLVESIPEGLDFPNASTGNPSTSQAWLG LLAGAHSSLDIASFYWTLTNNDTHTQEPSAQQGEEVLRQLQTLAPKGVNVRIAVSKPSG PQPQADLQALLQSGAQVRMVDMQKLTHGVLHTKFWVVDQTHFYLGSANMDWRSLTQ VKELGVVMYNCSCLARDLTKIFEAYWFLGQAGSSIPSTWPRFYDTRYNQETPMEICLNG TPALAYLASAPPPLCPSGRTPDLKALLNVVDNARSFIYVAVMNYLPTLEFSHPHRFWPAI DDGLRRATYERGVKVRLLISCWGHSEPSMRAFLLSLAALRDNHTHSDIQVKLFVVPADE AQARIPYARVNHNKYMVTERATYIGTSNWSGNYFTETAGTSLLVTQNGRGGLRSQLEAI FLRDWDSPYIHDLDTSADSVGNACRLL

SEQID No:134

MRYFLLRPETLFLLCISLALWSYFFHTDEVKTIVKSSRDAVKMVKGKVAEIMQNDRLGGL DVLEAEFSKTWEFKNHNVAVYSIQGRRDHMEDRFEVLTDLANKTHPSIFGIFDGHGGE GGIRGAALRFFPTLSTLQVQSGQLTGAPRWPLVFTRISERDLDVPGLCRGGYARKGGG ALTSPLRPGGLRGADVVLLLDSFVCGSSGSRR

SEQID No:135

MEKQPQNSRRGLAPREVPPAVGLLIMALMNTLLYLCLDHFFIAPRQSTVDPTHCPYGH FRIGQMKNCSPWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALSQLTSLEMKD DFLHGLQMLKSLQGTHVVTLLGYCEDDNTMLTEYHPLGSLSNLEETLNLSKYQNVNTW QHRLELAMDYVSIINYLHHSPVGTRVMCDSNDLPKTLSQYLLTSNFSILANDLDALPLVN HSSGMLVKCGHRELHGDFVAPEQLWPYGEDVPFHDDLMPSYDEKIDIWKIPDISSFLLG HIEGSDMVRFHLFDIHKACKSQTPSERPTAQDVLETYQKVLDTLRDAMMSQAREML

SEQID No:136

MQRAGSSGGRGECDISGAGRLGLEEAARLSCAVHTSPGGGRRPGQAAGMSAKERPK
GKVIKDSVTLLPCFYFVELPILASSVVSLYFLELTDVFKPVHSGFSCYDRSLSMPYIEPTQ
EAIPFLMLLSLAFAGPAITIMVGEGILYCCLSKRRNGVGLEPNINAGGCNFNSFLRRAVRF
VGVHVFGLCSTALITDIIQLSTGYQAPYFLTVCKPNYTSLNVSCKENSYIVEDICSGSDLT
VINSGRKSFPSQHATLAAFAAVYVSMYFNSTLTDSSKLLKPLLVFTFIICGIICGLTRITQY
KNHPVDVYCGFLIGGGIALYLGLYAVGNFLPSDESMFQHRDALRSLTDLNQDPNRLLSA
KNGSSSDGIAHTEGILNRNHRDASSLTNLKRANADVEIITPRSPMGKENMVTFSNTLPRA
NTPSVEDPVRRNASIHASMDSARSKQLLTQWKNKNESRKLSLQVIEPEPGQSPPRSIE
MRSSSEPSRVGVNGDHHGPGNQYLKIQPGAVPGCNNSMPGGPRVSIQSRPGSSQLV
HIPEETQENISTSPKSSSARAKWLKAAEKTVACNRSNSQPRIMQVIAMSKQQGVLQSSP
KNTEGSTVSCTGSIRYKTLTDHEPSGIVRVEAHPENNRPIIQIPSTEGEGSGSWKWKAP
EKGSLRQTYELNDLNRDSESCESLKDSFGSGDRKRSNIDSNEHHHHGITTIRVTPVEGS
EIGSETLSISSSRDSTLRRKGNIILIPERSNSPENTRNIFYKGTSPTRAYKD

SEQID No:137

MLTTLKPFGSVSVESKMNNKAGSFFWNLRQFSTLVSTSRTMRLCCLGLCKPKIVHSNW NILNNFHNRMQSTDIIRYLFQDAFIFKSDVGFQTKGISTLTALRIERLLYAKRLFFDSKQSL VPVDKSDDELKKVNLNHEVSNEDVLTKETKPNRISSRKLSEECNSLSDVLDAFSKAPTF PSSNYFTAMWTIAKRLSDDQKRFEKRLMFSHPAFNQLCEHMMREAKIMQYKYLLFSLH AIVKLGIPQNTILVQTLLRVTQERINECDEICLSVLSTVLEAMEPCKNVHVLRTGFRILVDQ QVWKIEDVFTLQVVMKCIGKDAPIALKRKLEMKALRELDRFSVLNSQHMFEVLAAMNHR SLILLDECSKVVLDNIHGCPLRIMINILQSCKDLQYHNLDLFKGLADYVAATFDIWKFRKVL FILILFENLGFRPVGLMDLFMKRIVEDPESLNMKNILSILHTYSSLNHVYKCQNKEQFVEV MASALTGYLHTISSENLLDAVYSFCLMNYFPLAPFNQLLQKDIISELLTSDDMKNAYKLHT LDTCLKLDDTVYLRDIALSLPQLPRELPSSHTNAKVAEVLSSLLGGEGHFSKDVHLPHNY HIDFEIRMDTNRNQVLPLSDVDTTSATDIQRVAVLCVSRSAYCLGSSHPRGFLAMKMRH LNAMGFHVILVNNWEMDKLEMEDAVTFLKTKIYSVEALPVAAVNVQSTQ

SEQID No:138

RVYADAPAKLLLPPPAAWDLAVRLRGAEAASERQVYSVTMKLLLLHPAFQSCLLLTLLG

LWRTTPEAHASSLGAPAISAASFLQDLIHRYGEGDSLTLQQLKALLNHLDVGVGRGNVT QHVQGHRNLSTCFSSGDLFTAHNFSEQSRIGSSELQEFCPTILQQLDSRACTSENQEN EENEQTEEGRPSAVEVWGYGLLCVTVISLCSLLGASVVPFMKKTFYKRLLLYFIALAIGTL YSNALFQLIPEAFGFNPLEDYYVSKSAVVFGGFYLFFFTEKILKILLKQKNEHHHGHSHYA SESLPSKKDQEEGVMEKLQNGDLDHMIPQHCSSELDGKAPMVDEKVIVGSLSVQDLQA SQSACYWLKGVRYSDIGTLAWMITLSDGLHNFIDGLAIGASFTVSVFQGISTSVAILCEEF PHELGDFVILLNAGMSIQQALFFNFLSACCCYLGLAFGILAGSHFSANWIFALAGGMFLYI SLADMFPEMNEVCQEDERKGSILIPFIIQNLGLLTGFTIMVVLTMYSGQIQIG

SEQID No:139

MAAEWASRFWLWATLLIPAAAVYEDQVGKFDWRQQYVGKVKFASLEFSPGSKKLVVA TEKNVIAALNSRTGEILWRHVDKGTAEGAVDAMLLHGQDVITVSNGGRIMRSWETNIGG LNWEITLDSGSFQALGLVGLQESVRYIAVLKKTTLALHHLSSGHLKWVEHLPESDSIHYQ MVYSYGSGVVWALGVVPFSHVNIVKFNVEDGEIVQQVRVSTPWLQHLSGACGVVDEA VLVCPDPSSRSLQTLALETEWELRQIPLQSLDLEFGSGFQPRVLPTQPNPVDASRAQFF LHLSPSHYALLQYHYGTLSLLKNFPQTALVSFATTGEKTVAAVMACRNEVQKSSSSEDG SMGSFSEKSSSKDSLACFNQTYTINLYLVETGRRLLDTTITFSLEQSGTRPERLYIQVFLK KDDSVGYRALVQTEDHLLLFLQQLAGKVVLWSREESLAEVVCLEMVDLPLTGAQAELE GEFGKKADGLLGMFLKRLSSQLILLQAWTSHLWKMFYDARKPRSQIKNEINIDTLARDEF NLQKMMVMVTASGKLFGIESSSGTILWKQYLPNVKPDSSFKLMVQRTTAHFPHPPQCT LLVKDKESGMSSLYVFNPIFGKWSQVAPPVLKRPILQSLLLPVMDQDYAKVLLLIDDEYK VTAFPATRNVLRQLHELAPSIFFYLVDAEQGRLCGYRLRKDLTTELSWELTIPPEVQRIV KVKGKRSSEHVHSQGRVMGDRSVLYKSLNPNLLAVVTESTDAHHERTFIGIFLIDGVTG RIIHSSVQKKAKGPVHIVHSENWVVYQYWNTKARRNEFTVLELYEGTEQYNATAFSSLD RPQLPQVLQQSYIFPSSISAMEATITERGITSRHLLIGLPSGAILSLPKALLDPRRPEIPTE QSREENLIPYSPDVQIHAERFINYNQTVSRMRGIYTAPSGLESTCLVVAYGLDIYQTRVY **PSKQFDVLKDDYDYVLISSVLFGLVFATMITKRLAQVKLLNRAWR**

SEQID No:140

MAKVSELYDVTWEEMRDKMRKWREENSRNSEQIVEVGEELINEYASKLGDDIWIIYEQV MIAALDYGRDDLALFCLQELRRQFPGSHRVKRLTGMRFEAMERYDDAIQLYDRILQEDP TNTAARKRKIAIRKAQGKNVEAIRELNEYLEQFVGDQEAWHELAELYINEHDYAKAAFCL EELMMTNPHNHLYCQQYAEVKYTQGGLENLELSRKYFAQALKLNNRNMRALFGLYMS ASHIASNPKASAKTKKDNMKYASWAASQINRAYQFAGRSKKETKYSLKAVEDMLETLQI TQS

SEQID No:141

MWSIGAGALGAAALALLLANTDVFLSKPQKAALEYLEDIDLKTLEKEPRTFKAKELWEKN GAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDFQPYFKGEI FLDEKKKFYGPQRRKMMFMGFIRLGVWYNFFRAWNGGFSGNLEGEGFILGGVFVVGS GKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

SEQID No:142

MTLIEGVGDEVTVLFSVLACLLVLALAWVSTHTAEGGDPLPQPSGTPTPSQPSAAMAAT DSMRGEAPGAETPSLRHRGQAAQPEPSTGFTATPPAPDSPQEPLVLRLKFLNDSEQVA RAWPHDTIGSLKRTQFPGREQQVRLIYQGQLLGDDTQTLGSLHLPPNCVLHCHVSTRV GPPNPPCPPGSEPGPSGLEIGSLLLPLLLLLLLLLLWYCQIQYRPFFPLTATLGLAGFTLLL SLLAFAMYRP

SEQID No:143

MASGSNWLSGVNVVLVMAYGSLVFVLLFIFVKRQIMRFAMKSRRGPHVPVGHNAPKDL KEEIDIRLSRVQDIKYEPQLLADDDARLLQLETQGNQSCYNYLYRMKALDAIRTSEIPFHS EGRHPRSLMGKNFRSYLLDLRNTSTPFKGVRKALIDTLLDGYETARYGTGVFGQNEYL RYQEALSELATAVKARIGSSQRHHQSAAKDLTQSPEVSPTTIQVTYLPSSQKSKRAKHF LELKSFKDNYNTLESTL

SEQID No:144

MTARGLALGLLLLLCPAQVFSQSCVWYGECGIAYGDKRYNCEYSGPPKPLPKDGYDL VQELCPGFFFGNVSLCCDVRQLQTLKDNLQLPLQFLSRCPSCFYNLLNLFCELTCSPRQ SQFLNVTATEDYVDPVTNQTKTNVKELQYYVGQSFANAMYNACRDVEAPSSNDKALGL LCGKDADACNATNWIEYMFNKDNGQAPFTITPVFSDFPVHGMEPMNNATKGCDESVD EVTAPCSCQDCSIVCGPKPQPPPPAPWTILGLDAMYVIMWITYMAFLLVFFGAFFAVW CYRKRYFVSEYTPIDSNIAFSVNASDKGEASCCDPVSAAFEGCLRRLFTRWGSFCVRN PGCVIFFSLVFITACSSGLVFVRVTTNPVDLWSAPSSQARLEKEYFDQHFGPFFRTEQLII RAPLTDKHIYQPYPSGADVPFGPPLDIQILHQVLDLQIAIENITASYDNETVTLQDICLAPL SPYNTNCTILSVLNYFQNSHSVLDHKKGDDFFVYADYHTHFLYCVRAPASLNDTSLLHD PCLGTFGGPVFPWLVLGGYDDQNYNNATALVITFPVNNYYNDTEKLQRAQAWEKEFIN

FVKNYKNPNLTISFTAERSIEDELNRESDSDVFTVVISYAIMFLYISLALGHIKSCRRLLVD SKVSLGIAGILIVLSSVACSLGVFSYIGLPLTLIVIEVIPFLVLAVGVDNIFILVQAYQRDERL QGETLDQQLGRVLGEVAPSMFLSSFSETVAFFLGALSVMPAVHTFSLFAGLAVFIDFLL QITCFVSLLGLDIKRQEKNRLDIFCCVRGAEDGTSVQASESCLFRFFKNSYSPLLLKDW MRPIVIAIFVGVLSFSIAVLNKVDIGLDQSLSMPDDSYMVDYFKSISQYLHAGPPVYFVLE EGHDYTSSKGQNMVCGGMGCNNDSLVQQIFNAAQLDNYTRIGFAPSSWIDDYFDWVK PQSSCCRVDNITDQFCNASVVDPACVRCRPLTPEGKQRPQGGDFMRFLPMFLSDNPN PKCGKGGHAAYSSAVNILLGHGTRVGATYFMTYHTVLQTSADFIDALKKARLIASNVTET MGINGSAYRVFPYSVFYVFYEQYLTIIDDTIFNLGVSLGAIFLVTMVLLGCELWSAVIMCA TIAMVLVNMFGVMWLWGISLNAVSLVNLVMSCGISVEFCSHITRAFTVSMKGSRVERAE EALAHMGSSVFSGITLTKFGGIVVLAFAKSQIFQIFYFRMYLAMVLLGATHGLIFLPVLLSY IGPSVNKAKSCATEERYKGTERERLLNF

SEQID No:145

MSGCGLFLRTTAAARACRGLVVSTANRRLLRTSPPVRAFAKELFLGKIKKKEVFPFPEV SQDELNEINQFLGPVEKFFTEEVDSRKIDQEGKIPDETLEKLKSLGLFGLQVPEEYGGLG FSNTMYSRLGEIISMDGSITVTLAAHQAIGLKGIILAGTEEQKAKYLPKLASGEHIAAFCLT EPASGSDAASIRSRATLSEDKKHYILNGSKVWITNGGLANIFTVFAKTEVVDSDGSVKDK ITAFIVERDFGGVTNGKPEDKLGIRGSNTCEVHFENTKIPVENILGEVGDGFKVAMNILNS GRFSMGSVVAGLLKRLIEMTAEYACTRKQFNKRLSEFGLIQEKFALMAQKAYVMESMT YLTAGMLDQPGFPDCSIEAAMVKVFSSEAAWQCVSEALQILGGLGYTRDYPYERILRDT RILLIFEGTNEILRMYIALTGLQHAGRILTTRIHELKQAKVSTVMDTVGRRLRDSLGRTVDL GLTGNHGVVHPSLADSANKFEENTYCFGRTVETLLLRFGKTIMEEQLVLKRVANILINLY GMTAVLSRASRSIRIGLRNHDHEVLLANTFCVEAYLQNLFSLSQLDKYAPENLDEQIKKV SQQILEKRAYICAHPLDRTC

SEQID No:146

LERRWRRREAGAGAEAAAGSARPLGRQAAAARGSSPEAGAAAMAESIIIRVQSPDGV KRITATKRETAATFLKKVAKEFGFQNNGFSVYINRNKTGEITASSNKSLNLLKIKHGDLLF LFPSSLAGPSSEMETSVPPGFKVFGAPNVVEDEIDQYLSKQDGKIYRSRDPQLCRHGPL GKCVHCVPLEPFDEDYLNHLEPPVKHMSFHAYIRKLTGGADKGKFVALENISCKIKSGC EGHLPWPNGICTKCQPSAITLNRQKYRHVDNIMFENHTVADRFLDFWRKTGNQHFGYL YGRYTEHKDIPLGIRAEVAAIYEPPQIGTQNSLELLEDPKAEVVDEIAAKLGLRKVGWIFT DLVSEDTRKGTVRYSRNKDTYFLSSEECITAGDFQNKHPNMCRLSPDGHFGSKFVTAV

ATGGPDNQVHFEGYQVSNQCMALVRDECLLPCKDAPELGYAKESSSEQYVPDVFYKD VDKFGNEITQLARPLPVEYLIIDITTTFPKDPVYTFSISQNPFPIENRDVLGETQDFHSLAT YLSQNTSSVFLDTISDFHLLLFLVTNEVMPLQDSISLLLEAVRTRNEELAQTWKRSEQWA TIEQLCSEYPHPLPRHPVAGAGEQPTLHSSPLPVVPWIPHPAASWQVPSAMQRVETRP PCQARGRLR

SEQID No:147

MATAGGSGADPGSRGLLRLLSFCVLLAGLCRGNSVERKIYIPLNKTAPCVRLLNATHQI
GCQSSISGDTGVIHVVEKEEDLQWVLTDGPNPPYMVLLESKHFTRDLMEKLKGRTSRIA
GLAVSLTKPSPASGFSPSVQCPNDGFGVYSNSYGPEFAHCREIQWNSLGNGLAYEDFS
FPIFLLEDENETKVIKQCYQDHNLSQNGSAPTFPLCAMQLFSHMHAVISTATCMRRSSIQ
STFSINPEIVCDPLSDYNVWSMLKPINTTGTLKPDDRVVVAATRLDSRSFFWNVAPGAE
SAVASFVTQLAAAEALQKAPDVTTLPRNVMFVFFQGETFDYIGSSRMVYDMEKGKFPV
QLENVDSFVELGQVALRTSLELWMHTDPVSQKNESVRNQVEDLLATLEKSGAGVPAVI
LRRPNQSQPLPPSSLQRFLRARNISGVVLADHSGAFHNKYYQSIYDTAENINVSYPEWL
SPEEDLNFVTDTAKALADVATVLGRALYELAGGTNFSDTVQADPQTVTRLLYGFLIKAN
NSWFQSILRQDLRSYLGDGPLQHYIAVSSPTNTTYVVQYALANLTGTVVNLTREQCQDP
SKVPSENKDLYEYSWVQGPLHSNETDRLPRCVRSTARLARALSPAFELSQWSSTEYST
WTESRWKDIRARIFLIASKELELITLTVGFGILIFSLIVTYCINAKADVLFIAPREPGAVSY

SEQID No:148

MPSAKQRGSKGGHGAASPSEKGAHPSGGADDVAKKPPPAPQQPPPPAPHPQQHPQ
QHPQNQAHGKGGHRGGGGGGKSSSSSSASAAAAAAAASSSASCSRRLGRALNFLF
YLALVAAAAFSGWCVHHVLEEVQQVRRSHQDFSRQREELGQGLQGVEQKVQSLQATF
GTFESILRSSQHKQDLTEKAVKQGESEVSRISEVLQKLQNEILKDLSDGIHVVKDARERD
FTSLENTVEERLTELTKSINDNIAIFTEVQKRSQKEINDMKAKVASLEESEGNKQDLKALK
EAVKEIQTSAKSREWDMEALRSTLQTMESDIYTEVRELVSLKQEQQAFKEAADTERLAL
QALTEKLLRSEESVSRLPEEIRRLEEELRQLKSDSHGPKEDGGFRHSEAFEALQQKSQ
GLDSRLQHVEDGVLSMQVASARQTESLESLLSKSQEHEQRLAALQGRLEGLGSSEAD
QDGLASTVRSLGETQLVLYGDVEELKRSVGELPSTVESLQKVQEQVHTLLSQDQAQAA
RLPPQDFLDRLSSLDNLKASVSQVEADLKMLRTAVDSLVAYSVKIETNENNLESAKGLL
DDLRNDLDRLFVKVEKIHEKV

MFRNQYDNDVTVWSPQGRIHQIEYAMEAVKQGSATVGLKSKTHAVLVALKRAQSELAA HQKKILHVDNHIGISIAGLTADARLLCNFMRQECLDSRFVFDRPLPVSRLVSLIGSKTQIP TQRYGRRPYGVGLLIAGYDDMGPHIFQTCPSANYFDCRAMSIGARSQSARTYLERHMS EFMECNLNELVKHGLRALRETLPAEQDLTTKNVSIGIVGKDLEFTIYDDDDVSPFLEGLE ERPQRKAQPAQPADEPAEKADEPMEH

SEQID No:150

SSIGTGYDLSASTFSPDGRVFQVEYAMKAVENSSTAIGIRCKDGVVFGVEKLVLSKLYEE GSNKRLFNVDRHVGMAVAGLLADARSLADIAREEASNFRSNFGYNIPLKHLADRVAMY VHAYTLYSAVRPFGCSFMLGSYSVNDGAQLYMIDPSGVSYGYWGCAIGKARQAAKTEI EKLQMKEMTCRDIVKEVAKIIYIVHDEVKDKAFELELSWVGELTNGRHEIVPKDIREEAEK YAKESLKEEDESDDDNM

SEQID No:151

MSRRYDSRTTIFSPEGRLYQVEYAMEAIGHAGTCLGILANDGVLLAAERRNIHKLLDEVF FSEKIYKLNEDMACSVAGITSDANVLTNELRLIAQRYLLQYQEPIPCEQLVTALCDIKQAY TQFGGKRPFGVSLLYIGWDKHYGFQLYQSDPSGNYGGWKATCIGNNSAAAVSMLKQD YKEGEMTLKSALALAIKVLNKTMDVSKLSAEKVEIATLTRENGKTVIRVLKQKEVEQLIKK HEEEEAKAEREKKEKEQKEKDK

SEQID No:152

MSRGSSAGFDRHITIFSPEGRLYQVEYAFKAINQGGLTSVAVRGKDCAVIVTQKKVPDK LLDSSTVTHLFKITENIGCVMTGMTADSRSQVQRARYEAANWKYKYGYEIPVDMLCKRI ADISQVYTQNAEMRPLGCCMILIGIDEEQGPQVYKCDPAGYYCGFKATAAGVKQTESTS FLEKKVKKKFDWTFEQTVETAITCLSTVLSIDFKPSEIEVGVVTVENPKFRILTEAEIDAHL VALAERD

SEQID No:153

MLSSTAMYSAPGRDLGMEPHRAAGPLQLRFSPYVFNGGTILAIAGEDFAIVASDTRLSE GFSIHTRDSPKCYKLTDKTVIGCSGFHGDCLTLTKIIEARLKMYKHSNNKAMTTGAIAAM LSTILYSRRFFPYYVYNIIGGLDEEGKGAVYSFDPVGSYQRDSFKAGGSASAMLQPLLD NQVGFKNMQNVEHVPLSLDRAMRLVKDVFISAAERDVYTGDALRICIVTKEGIREETVSL RKD

MEYLIGIQGPDYVLVASDRVAASNIVQMKDDHDKMFKMSEKILLLCVGEAGDTVQFAEYI QKNVQLYKMRNGYELSPTAAANFTRRNLADCLRSRTPYHVNLLLAGYDEHEGPALYYM DYLAALAKAPFAAHGYGAFLTLSILDRYYTPTISRERAVELLRKCLEELQKRFILNLPTFSV RIIDKNGIHDLDNISFPKQGS

SEQID No:155______

MSIMSYNGGAVMAMKGKNCVAIAADRRFGIQAQMVTTDFQKIFPMGDRLYIGLAGLATD VQTVAQRLKFRLNLYELKEGRQIKPYTLMSMVANLLYEKRFGPYYTEPVIAGLDPKTFKP FICSLDLIGCPMVTDDFVVSGTCAEQMYGMCESLWEPNMDPDHLFETISQAMLNAVDR DAVSGMGVIVHIIEKDKITTRTLKARMD

SEQID No:156

MEAFLGSRSGLWAGGPAPGQFYRIPSTPDSFMDPASALYRGPITRTQNPMVTGTSVLG VKFEGGVVIAADMLGSYGSLARFRNISRIMRVNNSTMLGASGDYADFQYLKQVLGQMVI DEELLGDGHSYSPRAIHSWLTRAMYSRRSKMNPLWNTMVIGGYADGESFLGYVDMLG VAYEAPSLATGYGAYLAQPLLREVLEKQPVLSQTEARDLVERCMRVLYYRDARSYNRF QTATVTEKGVEIEGPLSTETNWDIAHMISGFE

SEQID No:157

MALASVLERPLPVNQRGFFGLGGRADLLDLGPGSLSDGLSLAAPGWGVPEEPGIEMLH GTTTLAFKFRHGVIVAADSRATAGAYIASQTVKKVIEINPYLLGTMAGGAADCSFWERLL ARQCRIYELRNKERISVAAASKLLANMVYQYKGMGLSMGTMICGWDKRGPGLYYVDSE GNRISGATFSVGSGSVYAYGVMDRGYSYDLEVEQAYDLARRAIYQATYRDAYSGGAVN LYHVREDGWIRVSSDNVADLHEKYSGSTP

SEQID No:158

MAATLLAARGAGPAPAWGPEAFTPDWESREVSTGTTIMAVQFDGGVVLGADSRTTTG SYIANRVTDKLTPIHDRIFCCRSGSAADTQAVADAVTYQLGFHSIELNEPPLVHTAASLFK EMCYRYREDLMAGIIIAGWDPQEGGQVYSVPMGGMMVRQSFAIGGSGSSYIYGYVDA TYREGMTKEECLQFTANALALAMERDGSSGGVIRLAAIAESGVERQVLLGDQIPKFAVA TLPPA

MGQSQSGGHGPGGGKKDDKDKKKKYEPPVPTRVGKKKKKTKGPDAASKLPLVTPHT QCRLKLLKLERIKDYLLMEEEFIRNQEQMKPLEEKQEEERSKVDDLRGTPMSVGTLEEII DDNHAIVSTSVGSEHYVSILSFVDKDLLEPGCSVLLNHKVHAVIGVLMDDTDPLVTVMKV EKAPQETYADIGGLDNQIQEIKESVELPLTHPEYYEEMGIKPPKGVILYGPPGTGKTLLAK AVANQTSATFLRVVGSELIQKYLGDGPKLVRELFRVAEEHAPSIVFIDEIDAIGTKRYDSN SGGEREIQRTMLELLNQLDGFDSRGDVKVIMATNRIETLDPALIRPGRIDRKIEFPLPDEK TKKRIFQIHTSRMTLADDVTLDDLIMAKDDLSGADIKAICTEAGLMALRERRMKVTNEDF KKSKENVLYKKQEGTPEGLYL

SEQID No:160

MPDYLGADQRKTKEDEKDDKPIRALDEGDIALLKTYGQSTYSRQIKQVEDDIQQLLKKIN ELTGIKESDTGLAPPALWDLAADKQTLQSEQPLQVARCTKIINADSEDPKYIINVKQFAKF VVDLSDQVAPTDIEEGMRVGVDRNKYQIHIPLPPKIDPTVTMMQVEEKPDVTYSDVGGC KEQIEKLREVVETPLLHPERFVNLGIEPPKGVLLFGPPGTGKTLCARAVANRTDACFIRVI GSELVQKYVGEGARMVRELFEMARTKKACLIFFDEIDAIGGARFDDGAGGDNEVQRTM LELINQLDGFDPRGNIKVLMATNRPDTLDPALMRPGRLDRKIEFSLPDLEGRTHIFKIHAR SMSVERDIRFELLARLCPNSTGAEIRSVCTEAGMFAIRARRKIATEKDFLEAVNKVIKSYA KFSATPRYMTYN

SEQID No:161

MNLLPNIESPVTRQEKMATVWDEAEQDGIGEEVLKMSTEEIIQRTRLLDSEIKIMKSEVL RVTHELQAMKDKIKENSEKIKVNKTLPYLVSNVIELLDVDPNDQEEDGANIDLDSQRKGK CAVIKTSTRQTYFLPVIGLVDAEKLKPGDLVGVNKDSYLILETLPTEYDSRVKAMEVDER PTEQYSDIGGLDKQIQELVEAIVLPMNHKEKFENLGIQPPKGVLMYGPPGTGKTLLARAC AAQTKATFLKLAGPQLVQMFIGDGAKLVRDAFALAKEKAPSIIFIDELDAIGTKRFDSEKA GDREVQRTMLELLNQLDGFQPNTQVKVIAATNRVDILDPALLRSGRLDRKIEFPMPNEE ARARIMQIHSRKMNVSPDVNYEELARCTDDFNGAQCKAVCVEAGMIALRRGATELTHE DYMEGILEVQAKKKANLQYYA

SEQID No:162

MEEIGILVEKAQDEIPALSVSRPQTGLSFLGPEPEDLEDLYSRYKKLQQELEFLEVQEEYI KDEQKNLKKEFLHAQEEVKRIQSIPLVIGQFLEAVDQNTAIVGSTTGSNYYVRILSTIDRE LLKPNASVALHKHSNALVDVLPPEADSSIMMLTSDQKPDVMYADIGGMDIQKQEVREAV ELPLTHFELYKQIGIDPPRGVLMYGPPGCGKTMLAKAVAHHTTAAFIRVVGSEFVQKYL GEGPRMVRDVFRLAKENAPAIIFIDEIDAIATKRFDAQTGADREVQRILLELLNQMDGFD QNVNVKVIMATNRADTLDPALLRPGRLDRKIEFPLPDRRQKRLIFSTITSKMNLSEEVDL EDYVARPDKISGADINSICQESGMLAVRENRYIVLAKDFEKAYKTVIKKDEQEHEFYK

SEQID No:163

MALDGPEQMELEEGKAGSGLRQYYLSKIEELQLIVNDKSQNLRRLQAQRNELNAKVRLL REELQLLQEQGSYVGEVVRAMDKKKVLVKVHPEGKFVVDVDKNIDINDVTPNCRVALR NDSYTLHKILPNKVDPLVSLMMVEKVPDSTYEMIGGLDKQIKEIKEVIELPVKHPELFEAL GIAQPKGVLLYGPPGTGKTLLARAVAHHTDCTFIRVSGSELVQKFIGEGARMVRELFVM AREHAPSIIFMDEIDSIGSSRLEGGSGGDSEVQRTMLELLNQLDGFEATKNIKVIMATNRI DILDSALLRPGRIDRKIEFPPPNEEARLDILKIHSRKMNLTRGINLRKIAELMPGASGAEVK GVCTEAGMYALRERRVHVTQEDFEMAVAKVMQKDSEKNMSIKKLWK

SEQID No:164

MADPRDKALQDYRKKLLEHKEIDGRLKELREQLKELTKQYEKSENDLKALQSVGQIVGE VLKQLTEEKFIVKATNGPRYVVGCRRQLDKSKLKPGTRVALDMTTLTIMRYLPREVDPL VYNMSHEDPGNVSYSEIGGLSEQIRELREVIELPLTNPELFQRVGIIPPKGCLLYGPPGT GKTLLARAVASQLDCNFLKVVSSSIVDKYIGESARLIREMFNYARDHQPCIIFMDEIDAIG GRRFSEGTSADREIQRTLMELLNQMDGFDTLHRVKMIMATNRPDTLDPALLRPGRLDR KIHIDLPNEQARLDILKIHAGPITKHGEIDYEAIVKLSDGFNGADLRNVCTEAGMFAIRADH DFVVQEDFMKAVRKVADSKKLESKLDYKPV

SEQID No:165

MITSAAGIISLLDEDEPQLKEFALHKLNAVVNDFWAEISESVDKIEVLYEDEGFRSRQFAA LVASKVFYHLGAFEESLNYALGARDLFNVNDNSEYVETIIAKCIDHYTKQCVENADLPEG EKKPIDQRLEGIVNKMFQRCLDDHKYKQAIGIALETRRLDVFEKTILESNDVPGMLAYSL KLCMSLMQNKQFRNKVLRVLVKIYMNLEKPDFINVCQCLIFLDDPQAVSDILEKLVKEDN LLMAYQICFDLYESASQQFLSSVIQNLRTVGTPIASVPGSTNTGTVPGSEKDSDSMETE EKTSSAFVGKTPEASPEPKDQTLKMIKILSGEMAIELHLQFLIRNNNTDLMILKNTKDAVR NSVCHTATVIANSFMHCGTTSDQFLRDNLEWLARATNWAKFTATASLGVIHKGHEKEAL QLMATYLPKDTSPGSAYQEGGGLYALGLIHANHGGDIIDYLLNQLKNASNDIVRHGGSL GLGLAAMGTARQDVYDLLKTNLYQDDAVTGEAAGLALGLVMLGSKNAQAIEDMVGYAQ ETQHEKILRGLAVGIALVMYGRMEEADALIESLCRDKDPILRRSGMYTVAMAYCGSGNN

KAIRRLLHVAVSDVNDDVRSAAVESLGFILFRTPEQCPSVVSLLSESYNPHVRYGAAMA LGICCAGTGNKEAINLLEPMTNDPVNYVRQGALIASALIMIQQTEITCPKVNQFRQLYSKV INDKHDDVMAKFGAILAQGILDAGGHNVTISLQSRTGHTHMPSVVGVLVFTQFWFWFPL SHFLSLAYTPTCVIGLNKDLKMPKVQYKSNCKPSTFAYPAPLEVPKEKEKEKVSTAVLSI TAKAKKKEKEKEKKEEKMEVDEAEKKEEKEKKKEPEPNFQLLDNPARVMPAQLKVLT MPETCRYQPFKPLSIGGIIILKDTSEDIEELVEPVAAHGPKIEEEEQEPEPPEPFEYIDD

SEQID No:166

MAAAAVVEFQRAQSLLSTDREASIDILHSIVKRDIQENDEEAVQVKEQSILELGSLLAKTG QAAELGGLLKYVRPFLNSISKAKAARLVRSLLDLFLDMEAATGQEVELCLECIEWAKSEK RTFLRQALEARLVSLYFDTKRYQEALHLGSQLLRELKKMDDKALLVEVQLLESKTYHAL SNLPKARAALTSARTTANAIYCPPKLQATLDMQSGIIHAAEEKDWKTAYSYFYEAFEGYD SIDSPKAITSLKYMLLCKIMLNTPEDVQALVSGKLALRYAGRQTEALKCVAQASKNRSLA DFEKALTDYRAELRDDPIISTHLAKLYDNLLEQNLIRVIEPFSRVQIEHISSLIKLSKADVER KLSQMILDKKFHGILDQGEGVLIIFDEPPVDKTYEAALETIQNMSKVVDSLYNKAKKLT

SEQID No:167

MADGGSERADGRIVKMEVDYSATVDQRLPECAKLAKEGRLQEVIETLLSLEKQTRTASD MVSTSRILVAVVKMCYEAKEWDLLNENIMLLSKRRSQLKQAVAKMVQQCCTYVEEITDL PIKLRLIDTLRMVTEGKIYVEIERARLTKTLATIKEQNGDVKEAASILQELQVETYGSMEKK ERVEFILEQMRLCLAVKDYIRTQIISKKINTKFFQEENTEKLKLKYYNLMIQLDQHEGSYLS ICKHYRAIYDTPCIQAESEKWQQALKSVVLYVILAPFDNEQSDLVHRISGDKKLEEIPKYK DLLKLFTTMELMRWSTLVEDYGMELRKGSLESPATDVFGSTEEGEKRWKDLKNRVVE HNIRIMAKYYTRITMKRMAQLLDLSVDESEAFLSNLVVNKTIFAKVDRLAGIINFQRPKDP NNLLNDWSQKLNSLMSLVNKTTHLIAKEEMIHNLQ

SEQID No:168

MKDVPGFLQQSQNSGPGQPAVWHRLEELYTKKLWHQLTLQVLDFVQDPCFAQGDGLI KLYENFISEFEHRVNPLSLVEIILHVVRQMTDPNVALTFLEKTREKVKSSDEAVILCKTAIG ALKLNIGDLQVTKETIEDVEEMLNNLPGVTSVHSRFYDLSSKYYQTIGNHASYYKDALRF LGCVDIKDLPVSEQQERAFTLGLAGLLGEGVFNFGELLMHPVLESLRNTDRQWLIDTLY AFNSGNVERFQTLKTAWGQQPDLAANEAQLLRKIQLLCLMEMTFTRPANHRQLTFEEIA KSAKITVNEVELLVMKALSVGLVKGSIDEVDKRVHMTWVQPRVLDLQQIKGMKDRLEF WCTDVKSMEMLVEHQAHDILT

-MEEGGRDKAPVQPQQSPAAAPGGTDEKPSGKERRDAGDKDKEQELSEEDKQLQDEL **EMLVERLGEKDTSLYRPALEELRRQIRSSTTSMTSVPKPLKFLRPHYGKLKEIYENMAP** GENKRFAADIISVLAMTMSGERECLKYRLVGSQEELASWGHEYVRHLAGEVAKEWQEL DDAEKVQREPLLTLVKEIVPYNMAHNAEHEACDLLMEIEQVDMLEKDIDENAYAKVCLYL TSCVNYVPEPENSALLRCALGVFRKFSRFPEALRLALMLNDMELVEDIFTSCKDVVVQK _QMAFMLGRHGVFLELSEDVEEYEDLTEIMSNVQLNSNFLALARELDIMEPKVPDDIYKT HLENNRFGGSGSQVDSARMNLASSFVNGFVNAAFGQDKLLTDDGNKWLYKNKDHGM LSAAASLGMILLWDVDGGLTQIDKYLYSSEDYIKSGALLACGIVNSGVRNECDPALALLS DYVLHNSNTMRLGSIFGLGLAYAGSNREDVLTLLLPVMGDSKSSMEVAGVTALACGMIA VGSCNGDVTSTILQTIMEKSETELKDTYARWLPLGLGLNHLGKGEAIEAILAALEVVSEPF RSFANTLVDVCAYAGSGNVLKVQQLLHICSEHFDSKEKEEDKDKKEKKDKDKKEAPAD MGAHQGVAVLGIALIAMGEEIGAEMALRTFGHLLRYGEPTLRRAVPLALALISVSNPRLNI LDTLSKFSHDADPEVSYNSIFAMGMVGSGTNNARLAAMLRQLAQYHAKDPNNLFMVRL AQGLTHLGKGTLTLCPYHSDRQLMSQVAVAGLLTVLVSFLDVRNIILGKSHYVLYGLVAA MQPRMLVTFDEELRPLPVSVRVGQAVDVVGQAGKPKTITGFQTHTTPVLLAHGERAEL ATEEFLPVTPILEGFVILRKNPNYDL

SEQID No:170

MKQEGSARRRGADKAKPPPGGGEQEPPPPPAPQDVEMKEEAATGGGSTGEADGKTA
AAAAEHSQRELDTVTLEDIKEHVKQLEKAVSGKEPRFVLRALRMLPSTSRRLNHYVLYK
AVQGFFTSNNATRDFLLPFLEEPMDTEADLQFRPRTGKAASTPLLPEVEAYLQLLVVIFM
MNSKRYKEAQKISDDLMQKISTQNRRALDLVAAKCYYYHARVYEFLDKLDVVRSFLHAR
LRTATLRHDADGQATLLNLLLRNYLHYSLYDQAEKLVSKSVFPEQANNNEWARYLYYT
GRIKAIQLEYSEARRTMTNALRKAPQHTAVGFKQTVHKLLIVVELLLGEIPDRLQFRQPSL
KRSLMPYFLLTQAVRTGNLAKFNQVLDQFGEKFQADGTYTLIIRLRHNVIKTGVRMISLS
YSRISLADIAQKLQLDSPEDAEFIVAKAIRDGVIEASINHEKGYVQSKEMIDIYSTREPQLA
FHQRISFCLDIHNMSVKAMRFPPKSYNKDLESAEERREREQQDLEFAKEMAEDDDDSF
P

SEQID No:171

MVLESTMVCVDNSEYMRNGDFLPTRLQAQQDAVNIVCHSKTRSNPENNVGLITLANDC EVLTTLTPDTGRILSKLHTVQPKGKITFCTGIRVAHLALKHRQGKNHKMRIIAFVGSPVED

NEKDLVKLAKRLKKEKVNVDIINFGEEEVNTEKLTAFVNTLNGKDGTGSHLVTVPPGPSL ADALISSPILAGEGGAMLGLGASDFEFGVDPSADPELALALRVSMEEQRQRQEEEARR AAAASAAEAGIATTGTEDSDDALLKMTISQQEFGRTGLPDLSSMTEEEQIAYAMQMSLQ GAEFGQAESADIDASSAMDTSEPAKEEDDYDVMQDPEFLQSVLENLPGVDPNNEAIRN AMGSLASQATKDGKKDKKEEDKK

SEQID No:172

MLTFMASDSEEEVCDERTSLMSAESPTPRSCQEGRQGPEDGENTAQWRSQENEEDG EEDPDRYVCSGVPGRPPGLEEELTLKYGAKHVIMLFVPVTLCMIVVVATIKSVRFYTEKN GQLIYTPFTEDTPSVGQRLLNSVLNTLIMISVIVVMTIFLVVLYKYRCYKFIHGWLIMSSLM LLFLFTYIYLGEVLKTYNVAMDYPTLLLTVWNFGAVGMVCIHWKGPLVLQQAYLIMISAL MALVFIKYLPEWSAWVILGAISVYDLVAVLCPKGPLRMLVETAQERNEPIFPALIYSSAMV WTVGMAKLDPSSQGALQLPYDPEMEEDSYDSFGEPSYPEVFEPPLTGYPGEELEEEE ERGVKLGLGDFIFYSVLVGKAAATGSGDWNTTLACFVAILIGLCLTLLLLAVFKKALPALPI SITFGLIFYFSTDNLVRPFMDTLASHQLYI

SEQID No:173

MAAKVFESIGKFGLALAVAGGVVNSALYNVDAGHRAVIFDRFRGVQDIVVGEGTHFLIP WVQKPIIFDCRSRPRNVPVITGSKDLQNVNITLRILFRPVASQLPRIFTSIGEDYDERVLPS ITTEILKSVVARFDAGELITQRELVSRQVSDDLTERAATFGLILDDVSLTHLTFGKEFTEAV EAKQVAQQEAERARFVVEKAEQQKKAAIISAEGDSKAAELIANSLATAGDGLIELRKLEA AEDIAYQLSRSRNITYLPAGQSVLLQLPQ

SEQID No:174

MPLAQLADPWQKMAVESPSDSAENGQQIMDEPMGEEEINPQTEEVSIKEIAITHHVKEG HEKADPSQFELLKVLGQGSFGKVFLVKKISGSDARQLYAMKVLKKATLKVRDRVRTKM ERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDLFTRLSKEVMFTEEDVKFYLAELA LALDHLHSLGIIYRDLKPENILLDEEGHIKLTDFGLSKESIDHEKKAYSFCGTVEYMAPEV VNRRGHTQSADWWSFGVLMFEMLTGTLPFQGKDRKETMTMILKAKLGMPQFLSPEAQ SLLRMLFKRNPANRLGAGPDGVEEIKRHSFFSTIDWNKLYRREIHPPFKPATGRPEDTF YFDPEFTAKTPKDSPGIPPSANAHQLFRGFSFVAITSDDESQAMQTVGVHSIVQQLHRN SIQFTDGYEVKEDIGVGSYSVCKRCIHKATNMEFAVKIIDKSKRDPTEEIEILLRYGQHPNI ITLKDVYDDGKYVYVVTELMKGGELLDKILRQKFFSEREASAVLFTITKTVEYLHAQGVV HRDLKPSNILYVDESGNPESIRICDFGFAKQLRAENGLLMTPCYTANFVAPEVLKRQGY

DAACDIWSLGVLLYTMLTGYTPFANGPDDTPEEILARIGSGKFSLSGGYWNSVSDTAKD LVSKMLHVDPHQRLTAALVLRHPWIVHWDQLPQYQLNRQDAPHLVKGAMAATYSALN RNQSPVLEPVGRSTLAQRRGIKKITSTAL

SEQID No:175

SVTQPAGSVMGRWSLTASPVTLTSLLPMVTAGPAAGKSSSSTSWDTVLTAITCASTVQ
LISTTLGASASGARMPTTCCSGTTVFLTALQDTMQREELVKNATPPAEPARAEDLSPAP
HVTPTSCCPTLAPAAPPASLGTILMTIMFASTQSQWSIEVGVDDHFLDLQQKTSLFKKV
WPHQDVCVSTTCNTHCGSCDSQASCTSCRDPNKVLLFGECQYESCAPQYYLDFSTNT
CKAADRVLINELLGLRVDRKEDNLMQTFFLECDWSCSACSGPLKTDCLQCMDGYVLQD
GACVEQCLSSFYQDSGLCKNCDSYCLQCQGPHECTRCKGPFLLLEAQCVQECGKGYF
ADHAKHKCTACPQGCLQCSHRDRCHLCDHGFFLKSGLCVYNCVPGFSVHTSNETCSG
KIHTPSLHVNGSLILPIGSIKPLDFSLLNVQDQEGRVEDLLFHVVSTPTNGQLVLSRNGKE
VQLDKAGRFSWKDVNEKKVRFVHSKEKLRKGYLFLKISDQQFFSEPQLINIQAFSTQAP
YVLRNEVLHISRGERATITTQMLDIRDDDNPQDVVIEIIDPPLHGQLLQTLQSPATPIYQF
QLDELSRGLLHYAHDGSDSTSDVAVLQANDGHSFHNILFQVKTVPQNDRGLQLVANSM
VWVPEGGMLQITNRILQAEAPGASAEEIIYKITQDYPQFGEVVLLVNMPADSPADEGQH
LPDGRTATPTSTFTQQDINEGIVWYRHSGAPAQSDSFRFEVSSASNAQTRLESHMFNIA
ILPQTPEAPKVSLEASLHMTAREDGLTVIQPHSLSFINSEKPSGKIVYNITLPLHPNQGIIE
HRDHPHSPIRYFTQEDINQGKVMYRPPPAAPHLQELMAFSFA

SEQID No:176

MSSQPAGNQTSPGATEDYSYGSWYIDEPQGGEELQPEGEVPSCHTSIPPGLYHACLA SLSILVLLLAMLVRRRQLWPDCVRGRPGLPSPVDFLAGDRPRAVPAAVFMVLLSSLCL LLPDEDALPFLTLASAPSQDGKTEAPRGAWKILGLFYYAALYYPLAACATAGHTAAHLLG STLSWAHLGVQVWQRAECPQVPKIYKYYSLLASLPLLLGLGFLSLWYPVQLVRSFSRRT GAGSKGLQSSYSEEYLRNLLCRKKLGSSYHTSKHGFLSWARVCLRHCIYTPQPGFHLP LKLVLSATLTGTAIYQVALLLLVGVVPTIQKVRAGVTTDVSYLLASFGIVLSEDKQEVVELV KHHLWALEVCYISALVLSCLLTFLVLMRSLVTHRTNLRALHRGAALDLSPLHRSPHPSRQ AIFCWMSFSAYQTAFICLGLLVQQIIFFLGTTALAFLVLMPVLHGRNLLLFRSLESSWPFW LTLALAVILQNMAAHWVFLETHDGHPQLTNRRVLYAATFLLFPLNVLVGAMVATWRVLL SALYNAIHLGQMDLSLLPPRAATLDPGYYTYRNFLKIEVSQSHPAMTAFCSLLLQAQSLL PRTMAAPQDSLRPGEEDEGMQLLQTKDSMAKGARPGASRGRARWGLAYTLLHNPTL QVFRKTALLGANGAQP

MERPWGAADGLSRWPHGLGLLLLQLLPPSTLSQDRLDAPPPPAAPLPRWSGPIGVS WGLRAAAAGGAFPRGGRWRRSAPGEDEECGRVRDFVAKLANNTHQHVFDDLRGSVS LSWVGDSTGVILVLTTFHVPLVIMTFGQSKLYRSEDYGKNFKDITDLINNTFIRTEFGMAI GPENSGKVVLTAEVSGGSRGGRIFRSSDFAKNFVQTDLPFHPLTQMMYSPQNSDYLLA LSTENGLWVSKNFGGKWEEIHKAVCLAKWGSDNTIFFTTYANGSCKADLGALELWRTS DLGKSFKTIGVKIYSFGLGGRFLFASVMADKDTTRRIHVSTDQGDTWSMAQLPSVGQE QFYSILAANDDMVFMHVDEPGDTGFGTIFTSDDRGIVYSKSLDRHLYTTTGGETDFTNV TSLRGVYITSVLSEDNSIQTMITFDQGGRWTHLRKPENSECDATAKNKNECSLHIHASY SISQKLNVPMAPLSEPNAVGIVIAHGSVGDAISVMVPDVYISDDGGYSWTKMLEGPHYY TILDSGGIIVAIEHSSRPINVIKFSTDEGQCWQTYTFTRDPIYFTGLASEPGARSMNISIWG FTESFLTSQWVSYTIDFKDILERNCEEKDYTIWLAHSTDPEDYEDGCILGYKEQFLRLRK SSMCQNGRDYVVTKQPSICLCSLEDFLCDFGYYRPENDSKCVEQPELKGHDLEFCLYG REEHLTTNGYRKIPGDKCQGGVNPVREVKDLKKKCTSNFLSPEKQNSKSNSVPIILAIVG LMLVTVVAGVLIVKKYVCGGRFLVHRYSVLQQHAEANGVDGVDALDTASHTNKSGYHD DSDEDLLE

SEQID No:178

MPAHLLQDDISSSYTTTTTITAPPSRVLQNGGDKLETMPLYLEDDIRPDIKDDIYDPTYKD KEGPSPKVEYVWRNIILMSLLHLGALYGITLIPTCKFYTWLWGVFYYFVSALGITAGAHRL WSHRSYKARLPLRLFLIIANTMAFQNDVYEWARDHRAHHKFSETHADPHNSRRGFFFS HVGWLLVRKHPAVKEKGSTLDLSDLEAEKLVMFQRRYYKPGLLMMCFILPTLVPWYFW GETFQNSVFVATFLRYAVVLNATWLVNSAAHLFGYRPYDKNISPRENILVSLGAVGEGF HNYHHSFPYDYSASEYRWHINFTTFFIDCMAALGLAYDRKKVSKAAILARIKRTGDGNYK SG

SEQID No:179

MAAAAPGNGRASAPRLLLLFLVPLLWAPAAVRAGPDEDLSHRNKEPPAPAQQLQPQPV AVQGPEPARVEKIFTPAAPVHTNKEDPATQTNLGFIHAFVAAISVIIVSELGDKTFFIAAIM AMRYNRLTVLAGAMLALGLMTCLSVLFGYATTVIPRVYTYYVSTVLFAIFGIRMLREGLK MSPDEGQEELEEVQAELKKKDEEFQRTKLLNGPGDVETGTSITVPQKKWLHFISPIFVQ ALTLTFLAEWGDRSQLTTIVLAAREDPYGVAVGGTVGHCLCTGLAVIGGRMIAQKISVRT VTIIGGIVFLAFAFSALFISPDSGF

MTSIHFVVHPLPGTEDQLNDRLREVSEKLNKYNLNSHPPLNVLEQATIKQCVVGPNHAA FLLEDGRVCRIGFSVQPDRLELGKPDNNDGSKLNSNSGAGRTSRPGRTSDSPWFLSG SETLGRLAGNTLGSRWSSGVGGSGGGSSGRSSAGARDSRRQTRVIRTGRDRGSGLL GSQPQPVIPASVIPEELISQAQVVLQGKSRSVIIRELQRTNLDVNLAVNNLLSRDDEDGD DGDDTASESYLPGEDLMSLLDADIHSAHPSVIIDADAMFSEDISYFGYPSFRRSSLSRLG SSRVLLLPLERDSELLRERESVLRLRERRWLDGASFDNERGSTSKEGEPNLDKKNTPV QSPVSLGEDLQWWPDKDGTKFICIGALYSELLAVSSKGELYQWKWSESEPYRNAQNP SLHHPRATFLGLTNEKIVLLSANSIRATVATENNKVATWVDETLSSVASKLEHTAQTYSE LQGERIVSLHCCALYTCAQLENSLYWWGVVPFSQRKKMLEKARAKNKKPKSSAGISSM PNITVGTQVCLRNNPLYHAGAVAFSISAGIPKVGVLMESVWNMNDSCRFQLRSPESLKN MEKASKTTEAKPESKQEPVKTEMGPPPSPASTCSDASSIASSASMPYKRRRSTPAPKE EEKVNEEQWSLREVVFVEDVKNVPVGKVLKVDGAYVAVKFPGTSSNTNCQNSSGPDA DPSSLLQDCRLLRIDELQVVKTGGTPKVPDCFQRTPKKLCIPEKTEILAVNVDSKGVHAV LKTGNWVRYCIFDLATGKAEQENNFPTSSIAFLGQNERNVAIFTAGQESPIILRDGNGTIY PMAKDCMGGIRDPDWLDLPPISSLGMGVHSLINLPANSTIKKKAAVIIMAVEKQTLMQHIL RCDYEACRQYLMNLEQAVVLEQNLQMLQTFISHRCDGNRNILHACVSVCFPTSNKETK EEEEAERSERNTFAERLSAVEAIANAISVVSSNGPGNRAGSSSSRSLRLREMMRRSLR AAGLGRHEAGASSSDHQDPVSPPIAPPSWVPDPPAMDPDGDIDFILAPAVGSLTTAATG TGQGPSTSTIPGPSTEPSVVESKDRKANAHFILKLLCDSVVLQPYLRELLSAKDARGMT PFMSAVSGRAYPAAITILETAQKIAKAEISSSEKEEDVFMGMVCPSGTNPDDSPLYVLCC NDTCSFTWTGAEHINQDIFECRTCGLLESLCCCTECARVCHKGHDCKLKRTSPTAYCD CWEKCKCKTLIAGQKSARLDLLYRLLTATNLVTLPNSRGEHLLLFLVQTVARQTVEHCQ YRPPRIREDRNRKTASPEDSDMPDHDLEPPRFAQLALERVLQDWNALKSMIMFGSQEN KDPLSASSRIGHLLPEEQVYLNQQSGTIRLDCFTHCLIVKCTADILLLDTLLGTLVKELQN KYTPGRREEAIAVTMRFLRSVARVFVILSVEMASSKKKNNFIPQPIGKCKRVFQALLPYA VEELCNVAESLIVPVRMGIARPTAPFTLASTSIDAMQGSEELFSVEPLPPRPSSDQSSSS SQSQSSYIIRNPQQRRISQSQPVRGRDEEQDDIVSADVEEVEVVEGVAGEEDHHDEQE EHGEENAEAEGQHDEHDEDGSDMELDLLAAAETESDSESNHSNQDNASGRRSVVTAA TAGSEAGASSVPAFFSEDDSQSNDSSDSDSSSSQSDDIEQETFMLDEPLERTTNSSHA NGAAQAPRSMQWAVRNTQHQRAASTAPSSTSTPAASSAGLIYIDPSNLRRSGTISTSAA AAAAALEASNASSYLTSASSLARAYSIVIRQISDLMGLIPKYNHLVYSQIPAAVKLTYQDA VNLQNYVEEKLIPTWNWMVSIMDSTEAQLRYGSALASAGDPGHPNHPLHASQNSARR

ERMTAREEASLRTLEGRRRATLLSARQGMMSARGDFLNYALSLMRSHNDEHSDVLPV LDVCSLKHVAYVFQALIYWIKAMNQQTTLDTPQLERKRTRELLELGIDNEDSEHENDDD TNQSATLNDKDDDSLPAETGQNHPFFRRSDSMTFLGCIPPNPFEVPLAEAIPLADQPHL LQPNARKEDLFGRPSQGLYSSSASSGKCLMEVTVDRNCLEVLPTKMSYAANLKNVMN MQNRQKKEGEEQPVLPEETESSKPGPSAHDLAAQLKSSLLAEIGLTESEGPPLTSFRPQ CSFMGMVISHDMLLGRWRLSLELFGRVFMEDVGAEPGSILTELGGFEVKESKFRREME KLRNQQSRDLSLEVDRDRDLLIQQTMRQLNNHFGRRCATTPMAVHRVKVTFKDEPGE GSGVARSFYTAIAQAFLSNEKLPNLECIQNANKGTHTSLMQRLRNRGERDRERERERE MRRSSGLRAGSRRDRDRDFRRQLSIDTRPFRPASEGNPSDDPEPLPAHRQALGERLY PRVQAMQPAFASKITGMLLELSPAQLLLLLASEDSLRARVDEAMELIIAHGRENGADSIL DLGLVDSSEKVQQENRKRHGSSRSVVDMDLDDTDDGDDNAPLFYQPGKRGFYTPRP GKNTEARLNCFRNIGRILGLCLLQNELCPITLNRHVIKVLLGRKVNWHDFAFFDPVMYES LRQLILASQSSDADAVFSAMDLAFAIDLCKEEGGGQVELIPNGVNIPVTPQNVYEYVRKY AEHRMLVVAEQPLHAMRKGLLDVLPKNSLEDLTAEDFRLLVNGCGEVNVQMLISFTSFN DESGENAEKLLQFKRWFWSIVEKMSMTERQDLVYFWTSSPSLPASEEGFQPMPSITIR PPDDQHLPTANTCISRLYVPLYSSKQILKQKLLLAIKTKNFGFV

SEQID No:181

MATHGQTCARPMCIPPSYADLGKVARDIFNKGFGFGLVKLDVKTKSCSGVEFSTSGSS NTDTGKVTGTLETKYKWCEYGLTFTEKWNTDNTLGTEIAIEDQICQGLKLTFDTTFSPNT GKKSGKIKSSYKRECINLGCDVDFDFAGPAIHGSAVFGYEGWLAGYQMTFDSAKSKLT RNNFAVGYRTGDFQLHTNVNDGTEFGGSIYQKVCEDLDTSVNLAWTSGTNCTRFGIAA KYQLDPTASISAKVNNSSLIGVGYTQTLRPGVKLTLSALVDGKSINAGGHKVGLALELEA

SEQID No:182

MDSNTAPLGPSCPQPPPAPQPQARSRLNATASLEQERSERPRAPGPQAGPGPGVRD AAAPAEPQAQHTRSRERADGTGPTKGDMEIPFEEVLERAKAGDPKAQTEVGKHYLQLA GDTDEELNSCTAVDWLVLAAKQGRREAVKLLRRCLADRRGITSENEREVRQLSSETDL ERAVRKAALVMYWKLNPKKKKQVAVAELLENVGQVNEHDGGAQPGPVPKSLQKQRR MLERLVSSESKNYIALDDFVEITKKYAKGVIPSSLFLQDDEDDDELAGKSPEDLPLRLKV VKYPLHAIMEIKEYLIDMASRAGMHWLSTIIPTHHINALIFFFIISNLTIDFFAFFIPLVIFYLSF ISMVICTLKVFQDSKAWENFRTLTDLLLRFEPNLDVEQAEVNFGWNHLEPYAHFLLSVFF VIFSFPIASKDCIPCSELAVITGFFTVTSYLSLSTHAEPYTRRALATEVTAGLLSLLPSMPL NWPYLKVLGQTFITVPVGHLVVLNVSVPCLLYVYLLYLFFRMAQLRNFKGTYCYLVPYLV

CFMWCELSVVILLESTGLGLLRASIGYFLFLFALPILVAGLALVGVLQFARWFTSLELTKIA VTVAVCSVPLLLRWWTKASFSVVGMVKSLTRSSMVKLILVWLTAIVLFCWFYVYRSEGM KVYNSTLTWQQYGALCGPRAWKETNMARTQILCSHLEGHRVTWTGRFKYVRVTDIDN SAESAINMLPFFIGDWMRCLYGEAYPACSPGNTSTAEEELCRLKLLAKHPCHIKKFDRY KFEITVGMPFSSGADGSRSREEDDVTKDIVLRASSEFKSVLLSLRQGSLIEFSTILEGRLG SKWPVFELKAISCLNCMAQLSPTRRHVKIEHDWRSTVHGAVKFAFDFFFFPFLSAA

SEQID No:183

MGSGPLSLPLALSPPRLLLLLLLSLLPVARASEAEHRLFERLFEDYNEIIRPVANVSDPVII
HFEVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKP
DIVLYNNAVGDFQVDDKTKALLKYTGEVTWIPPAIFKSSCKIDVTYFPFDYQNCTMKFGS
WSYDKAKIDLVLIGSSMNLKDYWESGEWAIIKAPGYKHDIKYNCCEEIYPDITYSLYIRRL
PLFYTINLIIPCLLISFLTVLVFYLPSDCGEKVTLCISVLLSLTVFLLVITETIPSTSLVIPLIGEY
LLFTMIFVTLSIVITVFVLNVHYRTPTTHTMPSWVKTVFLNLLPRVMFMTRPTSNEGNAQ
KPRPLYGAELSNLNCFSRAESKGCKEGYPCQDGMCGYCHHRRIKISNFSANLTRSSSS
ESVDAVLSLSALSPEIKEAIQSVKYIAENMKAQNEAKEEQKAQEIQQLKRKEKSTETSDQ
EPGL

SEQID No:184 ·

MEKRETFVQAVSKELVGEFLQFVQLDKEASDPFSLNELLDELSRKQKEELWQRLKNLLT DVLLESPVDGWQVVEAQGEDNMETEHGSKMRKSIEIIYAITSVILASVSVINESENYEALL ECVIILNGILYALPESERKLQSSIQDLCVTWWEKGLPAKEDTGKTAFVMLLRRSLETKTG ADVCRLWRIHQALYCFDYDLEESGEIKDMLLECFININYIKKEEGRRFLSCLFNWNINFIK MIHGTIKNQLQGLQKSLMVYIAEIYFRAWKKASGKILEAIENDCIQDFMFHGIHLPRRSPV HSKVREVLSYFHHQKKVRQGVEEMLYRLYKPILWRGLKARNSEVRSNAALLFVEAFPIR DPNLHAIEMDSEIQKQFEELYSLLEDPYPMVRSTGILGVCKITSKYWEMMPPTILIDLLKK VTGELAFDTSSADVRCSVFKCLPMILDNKLSHPLLEQLLPALRYSLHDNSEKVRVAFVD MLLKIKAVRAAKFWKICPMEHILVRLETDSRPVSRRLVSLIFNSFLPVNQPEEVWCERCV TLVQMNHAAARRFYQYAHEHTACTNIAKLIHVIRHCLNACIQRAVREPPEDEEEEDGRE KENVTVLDKTLSVNDVACMAGLLEIIVILWKSIDRSMENNKEAKLYTINKFASVLPEYLKV FKDDRCKIPLFMLMSFMPASAVPPFSCGVISTLRSREEGAVDKSYCTLLDCLCSWGQV GHILELVDNWLPTEHAQAKSNTASKGRVQIHDTRPVKPELALVYIEYLLTHPKNRECLLS APRKKLNHLLKALETSKADLESLLQTPGGKPRGFSEAAAPRAFGLHCRLSIHLQHKFCS EGKVYLSMLEDTGFWLESKILSFIQDQEEDYLKLHRVIYQQIIQTYLTVCKDVVMVGLGD

HQFQMQLLQRSLGIMQTVKGFFYVSLLLDILKEITGSSLIQKTDSDEEVAMLLDTVQKVF QKMLECIARSFRKQPEEGLRLLYSVQRPLHEFITAVQSRHTDTPVHRGVLSTLIAGPVVE ISHQLRKVSDVEELTPPEHLSDLPPFSRCLIGIIIKSSNVVRSFLDELKACVASNDIEGIVCL TAAVHIILVINAGKHKSSKVREVAATVHRKLKTFMEITLEEDSIERFLYESSSRTLGELLNS

SEQID No:185

MAAAAVQGGRSGGSGGCSGAGGASNCGTGSGRSGLLDKWKIDDKPVKIDKWDGSAV KNSLDDSAKKVLLEKYKYVENFGLIDGRLTICTISCFFAIVALIWDYMHPFPESKPVLALC VISYFVMMGILTIYTSYKEKSIFLVAHRKDPTGMDPDDIWQLSSSLKRFDDKYTLKLTFIS GRTKQQREAEFTKSIAKFFDHSGTLVMDAYEPEISRLHDSLAIERKIK

SEQID No:186

MAVLRQLALLLWKNYTLQKRKVLVTVLELFLPLLFPGILIWLRLKIQSENVPNATIYPGQSI QELPLFFTFPPPGDTWELAYIPSHSDAAKTVTETVRRALVINMRVRGFPSEKDFEDYIRY DNCSSSVLAAVVFEHPFNHSKEPLPLAVKYHLRFSYTRRNYMWTQTGSFFLKETEGWH TTSLFPLFPNPGPRELTSPDGGEPGYIREGFLAVQHAVDRAIMEYHADAATRQLFQRLT VTIKRFPYPPFIADPFLVAIQYQLPLLLLLSFTYTALTIARAVVQEKERRLKEYMRMMGLS SWLHWSAWFLLFFLFLLIAASFMTLLFCVKVKPNVAVLSRSDPSLVLAFLLCFAISTISFSF MVSTFFSKANMAAAFGGFLYFFTYIPYFFVAPRYNWMTLSQKLCSCLLSNVAMAMGAQ LIGKFEAKGMGIQWRDLLSPVNVDDDFCFGQVLGMLLLDSVLYGLVTWYMEAVFPGQF GVPQPWYFFIMPSYWCGKPRAVAGKEEEDSDPEKALRNEYFEAEPEDLVAGIKIKHLSK VFRVGNKDRAAVRDLNLNLYEGQITVLLGHNGAGKTTTLSMLTGLFPPTSGRAYISGYEI SQDMVQIRKSLGLCPQHDILFDNLTVAEHLYFYAQLKGLSRQKCPEEVKQMLHIIGLEDK WNSRSRFLSGGMRRKLSIGIALIAGSKVLILDEPTSGMDAISRRAIWDLLQRQKSDRTIVL TTHFMDEADLLGDRIAIMAKGELQCCGSSLFLKQKYGAGYHMTLVKEPHCNPEDISQLV HHHVPNATLESSAGAELSFILPRESTHRFEGLFAKLEKKQKELGIASFGASITTMEEVFLR VGKLVDSSMDIQAIQLPALQYQHERRASDWAVDSNLCGAMDPSDGIGALIEEERTAVKL NTGLALHCQQFWAMFLKKAAYSWREWKMVAAQVLVPLTCVTLALLAINYSSELFDDPM LRLTLGEYGRTVVPFSVPGTSQLGQQLSEHLKDALQAEGQEPREVLGDLEEFLIFRASV **EGGGFNERCLVAASFRDVGERTVVNALFNNQAYHSPATALAVVDNLLFKLLCGPHASIV** VSNFPQPRSALQAAKDQFNEGRKGFDIALNLLFAMAFLASTFSILAVSERAVQAKHVQF VSGVHVASFWLSALLWDLISFLIPSLLLLVVFKAFDVRAFTRDGHMADTLLLLLLYGWAII PLMYLMNFFFLGAATAYTRLTIFNILSGIATFLMVTIMRIPAVKLEELSKTLDHVFLVLPNH CLGMAVSSFYENYETRRYCTSSEVAAHYCKKYNIQYQENFYAWSAPGVGRFVASMAA

SGCAYLILLFLIETNLLQRLRGILCALRRRRTLTELYTRMPVLPEDQDVADERTRILAPSP DSLLHTPLIIKELSKVYEQRVPLLAVDRLSLAVQKGECFGLLGFNGAGKTTTFKMLTGEE SLTSGDAFVGGHRISSDVGKVRQRIGYCPQFDALLDHMTGREMLVMYARLRGIPERHI GACVENTLRGLLLEPHANKLVRTYSGGNKRKLSTGIALIGEPAVIFLDEPSTGMDPVARR LLWDTVARARESGKAIIITSHSMEECEALCTRLAIMVQGQFKCLGSPQHLKSKFGSGYSL RAKVQSEGQQEALEEFKAFVDLTFPGSVLEDEHQGMVHYHLPGRDLSWAKVFGILEKA KEKYGVDDYSVSQISLEQVFLSFAHLQPPTAEEGR

SEQID No:187

MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRLPRETDEEPEEPGRR
GSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFAVGAAPHPFLHRYYQ
RQLSSTYRDLRKGVYVPYTQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGS
NWEGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAGFPLNQSEVLASVGG
SMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTN
LRLPKKVFEAAVKSIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVT
NQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRARKRI
GFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLP
LCLMVCQWRCLRCLRQQHDDFADDISLLK

SEQID No:188

MSEADGLRQRRPLRPQVVTDDDGQAPEAKDGSSFSGRVFRVTFLMLAVSLTVPLLGA
MMLLESPIDPQPLSFKEPPLLLGVLHPNTKLRQAERLFENQLVGPESIAHIGDVMFTGTA
DGRVVKLENGEIETIARFGSGPCKTRDDEPVCGRPLGIRAGPNGTLFVADAYKGLFEVN
PWKREVKLLLSSETPIEGKNMSFVNDLTVTQDGRKIYFTDSSSKWQRRDYLLLVMEGT
DDGRLLEYDTVTREVKVLLDQLRFPNGVQLSPAEDFVLVAETTMARIRRVYVSGLMKG
GADLFVENMPGFPDNIRPSSSGGYWVGMSTIRPNPGFSMLDFLSERPWIKRMIFKLFS
QETVMKFVPRYSLVLELSDSGAFRRSLHDPDGLVATYISEVHEHDGHLYLGSFRSPFLC
RLSLQAV

SEQID No:189

MLKVTVPSCSASSCSSVTASAAPGTASLVPDYWIDGSNRDALSDFFEVESELGRGATSI VYRCKQKGTQKPYALKVLKKTVDKKIVRTEIGVLLRLSHPNIIKLKEIFETPTEISLVLELVT GGELFDRIVEKGYYSERDAADAVKQILEAVAYLHENGIVHRDLKPENLLYATPAPDAPLK JADFGLSKIVEHQVLMKTVCGTPGYCAPEILRGCAYGPEVDMWSVGJITYILLCGFEPFY DERGDQFMFRRILNCEYYFISPWWDEVSLNAKDLVRKLIVLDPKKRLTTFQALQHPWVT GKAANFVHMDTAQKKLQEFNARRKLKAAVKAVVASSRLGSASSSHGSIQESHKASRDP SPIQDGNEDMKAIPEGEKIQGDGAQAAVKGAQAELMKVQALEKVKGADINAEEAPKMV PKAVEDGIKVADLELEEGLAEEKLKTVEEAAAPREGQGSSAVGFEVPQQDVILPEY

SEQID No:190

MSSSEEVSWISWFCGLRGNEFFCEVDEDYIQDKFNLTGLNEQVPHYRQALDMILDLEP DEELEDNPNQSDLIEQAAEMLYGLIHARYILTNRGIAQMLEKYQQGDFGYCPRVYCENQ PMLPIGLSDIPGEAMVKLYCPKCMDVYTPKSSRHHHTDGAYFGTGFPHMLFMVHPEYR PKRPANQFVPRLYGFKIHPMAYQLQLQAASNFKSPVKTIR

SEQID No:191

MWQLWASLCCLLVLANARSRPSFHPVSDELVNYVNKRNTTWQAGHNFYNVDMSYLKR LCGTFLGGPKPPQRVMFTEDLKLPASFDAREQWPQCPTIKEIRDQGSCGSCWAFGAV EAISDRICIHTNAHVSVEVSAEDLLTCCGSMCGDGCNGGYPAEAWNFWTRKGLVSGGL YESHVGCRPYSIPPCEHHVNGSRPPCTGEGDTPKCSKICEPGYSPTYKQDKHYGYNSY SVSNSEKDIMAEIYKNGPVEGAFSVYSDFLLYKSGVYQHVTGEMMGGHAIRILGWGVE NGTPYWLVANSWNTDWGDNGFFKILRGQDHCGIESEVVAGIPRTDQYWEKI

SEQID No:192

MMRQAPTARKTTTRRPKPTRPASTGVAGASSSLGPSGSASAGELSSSEPSTPAQTPLA
APIIPTPVLTSPGAVPPLPSPSKEEEGLRAQVRDLEEKLETLRLKRAEDKAKLKELEKHKI
QLEQVQEWKSKMQEQQADLQRRLKEARKEAKEALEAKERYMEEMADTADAIEMATLD
KEMAEERAESLQQEVEALKERVDELTTDLEILKAEIEEKGSDGAASSYQLKQLEEQNAR
LKDALVRMRDLSSSEKQEHVKLQKLMEKKNQELEVVRQQRERLQEELSQAESTIDELK
EQVDAALGAEEMVEMLTDRNLNLEEKVRELRETVGDLEAMNEMNDELQENARETELEL
REQLDMAGARVREAQKRVEAAQETVADYQQTIKKYRQLTAHLQDVNRELTNQQEASV
ERQQQPPPETFDFKIKFAETKAHAKAIEMELRQMEVAQANRHMSLLTAFMPDSFLRPG
GDHDCVLVLLLMPRLICKAELIRKQAQEKFELSENCSERPGLRGAAGEQLSFAAGLVYS
LSLLQATLHRYEHALSQCSVDVYKKVGSLYPEMSAHERSLDFLIELLHKDQLDETVNVE
PLTKAIKYYQHLYSIHLAEQPEDCTMQLADHIKFTQSALDCMSVEVGRLRAFLQGGQEA
TDIALLLRDLETSCSDIRQFCKKIRRRMPGTDAPGIPAALAFGPQVSDTLLDCRKHLTWV
VAVLQEVAAAAAQLIAPLAENEGLLVAALEELAFKASEQIYGTPSSSPYECLRQSCNILIS
TMNKLATAMQEGEYDAERPPSKPPPVELRAAALRAEITDAEGLGLKLEDRETVIKELKK

SLKIKGEELSEANVRLSLLEKKLDSAAKDADERIEKVQTRLEETQALLRKKEKEFEETMD ALQADIDQLEAEKAELKQRLNSQSKRTIEGLRGPPPSGIATLVSGIAGEEQQRGAIPGQA PGSVPGPGLVKDSPLLLQQISAMRLHISQLQHENSILKGAQMKASLASLPPLHVAKLSHE GPGSELPAGALYRKTSQLLETLNQLSTHTHVVDITRTSPAAKSPSAQLMEQVAQLKSLS DTVEKLKDEVLKETVSQRPGATVPTDFATFPSSAFLRAKEEQQDDTVYMGKVTFSCAA GFGQRHRLVLTQEQLHQLHSRLIS

SEQID No:193

MGKGGNQGEGAAEREVSVPTFSWEEIQKHNLRTDRWLVIDRKVYNITKWSIQHPGGQ RVIGHYAGEDATDAFRAFHPDLEFVGKFLKPLLIGELAPEEPSQDHGKNSKITEDFRALR KTAEDMNLFKTNHVFFLLLLAHIIALESIAWFTVFYFGNGWIPTLITAFVLATSQAQAGWL QHDYGHLSVYRKPKWNHLVHKFVIGHLKGASANWWNHRHFQHHAKPNIFHKDPDVNM LHVFVLGEWQPIEYGKKKLKYLPYNHQHEYFFLIGPPLLIPMYFQYQIIMTMIVHKNWVDL AWAVSYYIRFFITYIPFYGILGALLFLNFIRFLESHWFVWVTQMNHIVMEIDQEAYRDWFS SQLTATCNVEQSFFNDWFSGHLNFQIEHHLFPTMPRHNLHKIAPLVKSLCAKHGIEYQE KPLLRALLDIIRSLKKSGKLWLDAYLHK

SEQID No:194

MASLDRVKVLVLGDSGVGKSSLVHLLCQNQVLGNPSWTVGCSVDVRVHDYKEGTPEE KTCYIELWDVGGSVGSASSVKSTRAVFYNSVNGIIFVHDLTNKKSSQNLRRWSLEALNR DLVPTGVLVTNGDYDQEQFADNQIPLLVIGTKLDQIHETKRHEVLTTTAFLAEDFNPEEIN LDCTNPRYLAAGSSNAVKLSRFFDKVIEKRYFLREGNQIPGFPDRKRFGAGTLKSLHYD

SEQID No:195

MNNHVSSKPSTMKLKHTINPILLYFIHFLISLYTILTYIPFYFFSESRQEKSNRIKAKPVNSK PDSAYRSVNSLDGLASVLYPGCDTLDKVFTYAKNKFKNKRLLGTREVLNEEDEVQPNG KIFKKVILGQYNWLSYEDVFVRAFNFGNGLQMLGQKPKTNIAIFCETRAEWMIAAQACF MYNFQLVTLYATLGGPAIVHALNETEVTNIITSKELLQTKLKDIVSLVPRLRHIITVDGKPPT WSDFPKGIIVHTMAAVEALGAKASMENQPHSKPLPSDIAVIMYTSGSTGLPKGVMISHS NIIAGITGMAERIPELGEEDVYIGYLPLAHVLELSAELVCLSHGCRIGYSSPQTLADQSSKI KKGSKGDTSMLKPTLMAAVPEIMDRIYKNVMNKVSEMSSFQRNLFILAYNYKMEQISKG RNTPLCDSFVFRKVRSLLGGNIRLLLCGGAPLSATTQRFMNICFCCPVGQGYGLTESAG AGTISEVWDYNTGRVGAPLVCCEIKLKNWEEGGYFNTDKPHPRGEILIGGQSVTMGYY KNEAKTKADFSEDENGQRWLCTGDIGEFEPDGCLKIIDRKKDLVKLQAGEYVSLGKVEA

ALKNLPLVDNICAYANSYHSYVIGFVVPNQKELTELARKKGLKGTWEELCNSCEMENEV LKVLSEAAISASLEKFEIPVKIRLSPEPWTPETGLVTDAFKLKRKELKTHYQADIERMYGR K

SEQID No:196

MKLKLNVLTIILLPVHLLITIYSALIFIPWYFLTNAKKKNAMAKRIKAKPTSDKPGSPYRSVT HFDSLAVIDIPGADTLDKLFDHAVSKFGKKDSLGTREILSEENEMQPNGKVFKKLILGNY KWMNYLEVNRRVNNFGSGLTALGLKPKNTIAIFCETRAEWMIAAQTCFKYNFPLVTLYA TLGKEAVVHGLNESEASYLITSVELLESKLKTALLDISCVKHIIYVDNKAINKAEYPEGFEIH SMQSVEELGSNPENLGIPPSRPTPSDMAIVMYTSGSTGRPKGVMMHHSNLIAGMTGQ CERIPGLGPKDTYIGYLPLAHVLELTAEISCFTYGCRIGYSSPLTLSDQSSKIKKGSKGDC TVLKPTLMAAVPEIMDRIYKNVMSKVQEMNYIQKTLFKIGYDYKLEQIKKGYDAPLCNLLL FKKVKALLGGNVRMMLSGGAPLSPQTHRFMNVCFCCPIGQGYGLTESCGAGTVTEVT DYTTGRVGAPLICCEIKLKDWQEGGYTINDKPNPRGEIVIGGQNISMGYFKNEEKTAEDY SVDENGQRWFCTGDIGEFHPDGCLQIIDRKKDLVKLQAGEYVSLGKVEAALKNCPLIDNI CAFAKSDQSYVISFVVPNQKRLTLLAQQKGVEGTWVDICNNPAMEAEILKEIREAANAM KLERFEIPIKVRLSPEPWTPETGLVTDAFKLKRKELRNHYLKDIERMYGGK

SEQID No:197

MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPTGPEVQTPKPSDADWDDLWDQFDE RRYLNAKKWRVGDDPYKLYAFNQRESERISSNRAIPDTRHLSVLNRTPTHLIREIILVDDF SNDPDDCKQLIKLPKVKCLRNNERQGLVRSRIRGADIAQGTTLTFLDSHCEVNRDWLQP LLHRVKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWSLHFQWEQLSPEQKARRLDP TEPIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGENFEISFRVWMCGGSLEIVPCSRV GHVFRKKHPYVFPDGNANTYIKNTKRTAEVWMDEYKRYYYAARPFALERPFGNVESRL DLRKNLRCQSFKWYLENIYPELSIPKESSIQKGNIRQRQKCLESQANGTTGSSGQRPAG GTSEIWVQKPRVRNRRHAAPQGFDPGAKPSQHWRRPEHPAAE

SEQID No:198

MFFSMGFIVAVKGKIASPLEAPVFVAAPHSTFFDGIACVVAGLPSMVSRNENAQVPLIGR LLRAVQPVLVSRVDPDSRKNTINEIIKRTTSGGEWPQILVFPEGTCTNRSCLITFKPGAFI PGVPVQPVLLRYPNKLDTVTWTWQGYTFIQLCMLTFCQLFTKVEVEFMPVQVPNDEEK NDPVLFANKVRNLMAEALGIPVTDHTYEDCRLMISAGQLTLPMEAGLVEFTKISRKLKLD WDGVRKHLDEYASIASSSKGGRIGIEEFAKYLKLPVSDVLRQLFALFDRNHDGSIDFREY VIGLAVLCNPSNTEEIIQVAFKLFDVDEDGYITEEEFSTILQASLGVPDLDVSGLFKEIAQG DSISYEEFKSFALKHPEYAKIFTTYLDLQTCHVFSLPKEVQTTPSTASNKVSPEKHEEST SDKKDD

SEQID No:199

MRPRRPHQIADLFRPKDQIAYSDTSPFLILSEASLADLNSRLEKKVKATNFRPNIVISGCD VYAEDSWDELLIGDVELKRVMACSRCILTTVDPDTGVMSRKEPLETLKSYRQCDPSERK LYGKSPLFGQYFVLENPGTIKVGDPVYLLGQ

SEQID No:200

MSSFGYRTLTVALFTLICCPGSDEKVFEVHVRPKKLAVEPKGSLEVNCSTTCNQPEVGG LETSLNKILLDEQAQWKHYLVSNISHDTVLQCHFTCSGKQESMNSNVSVYQPPRQVILT LQPTLVAVGKSFTIECRVPTVEPLDSLTLFLFRGNETLHYETFGKAAPAPQEATATFNST ADREDGHRNFSCLAVLDLMSRGGNIFHKHSAPKMLEIYEPVSDSQMVIIVTVVSVLLSLF VTSVLLCFIFGQHLRQQRMGTYGVRAAWRRLPQAFRP

SEQID No:201

MDTEGFGELLQQAEQLAAETEGISELPHVERNLQEIQQAGERLRSRTLTRTSQETADVK
ASVLLGSRGLDISHISQRLESLSAATTFEPLEPVKDTDIQGFLKNEKDNALLSAIEESRKR
TFGMAEEYHRESMLVEWEQVKQRILHTLLASGEDALDFTQESEPSYISDVGPPGRSSL
DNIEMAYARQIYIYNEKIVNGHLQPNLVDLCASVAELDDKSISDMWTMVKQMTDVLLTPA
TDALKNRSSVEVRMEFVRQALAYLEQSYKNYTLVTVFGNLHQAQLGGVPGTYQLVRSF
LNIKLPAPLPGLQDGEVEGHPVWALIYYCMRCGDLLAASQVVNRAQHQLGEFKTWFQE
YMNSKDRRLSPATENKLRLHYRRALRNNTDPYKRAVYCIIGRCDVTDNQSEVADKTED
YLWLKLNQVCFDDDGTSSPQDRLTLSQFQKQLLEDYGESHFTVNQQPFLYFQVLFLTA
QFEAAVAFLFRMERLRCHAVHVALVLFELKLLLKSSGQSAQLLSHEPGDPPCLRRLNFV
RLLMLYTRKFESTDPREALQYFYFLRDEKDSQGENMFLRCVSELVIESREFDMILGKLE
NDGSRKPGVIDKFTSDTKPIINKVASVAENKGLFEEAAKLYDLAKNADKVLELMNKLLSP
VVPQISAPQSNKERLKNMALSIAERYRAQGISANKFVDSTFYLLLDLITFFDEYHSGHIDR
AFDIIERLKLVPLNQESVEERVAAFRNFSDEIRHNLSEVLLATMNILFTQFKRLKGTSPSS
SSRPQRVIEDRDSQLRSQARTLITFAGMIPYRTSGDTNARLVQMEVLMN

SEQID No:202

MLLVLECVLFSVAQGYFRMDSSATQFHIETHENTSGLWSIWYRNHFDRSVVLNDVFLSK

ETKHMLKILNFTGPLFLPPGCWNIFSLKLAVKDIAINLFTNVFLTTNIGAIFAIPLQIYSAPTK EGSLGFEVIAHCGMHYFMGKSKAGNPNWNGSLSLDQSTWNVDSELANKLYERWKKY KNGDVCKRNVLGTTRFAHLKKSKESESFVFFLPRLIAEPGLMLNFSATALRSRMIKYFVV QNPSSWPVSLQLLPLSLYPKPEALVHLLHRWFGTDMQMINFTTGEFQLTEACPYLGTH SEESRFGILHLHLQPLEMKRVGVVFTPADYGKVTSLILIRNNLTVIDMIGVEGFGARELLK VGGRLPGAGGSLRFKVPESTLMDCRRQLKDSKQILSITKNFKVENIGPLPITVSSLKINGY NCQGYGFEVLDCHQFSLDPNTSRDISIVFTPDFTSSWVIRDLSLVTAADLEFRFTLNVTL PHHLLPLCADVVPGPSWEESFWRLTVFFVSLSLLGVILIAFQQAQYILMEFMKTRQRQN ASSSSQQNNGPMDVISPHSYKSNCKNFLDTYGPSDKGRGKNCLPVNTPQSRIQNAAK RSPATYGHSQKKHKCSVYYSKHKTSTAAASSTSTTTEEKQTSPLGSSLPAAKEDICTDA MRENWISLRYASGINVNLQKNLTLPKNLLNKEENTLKNTIVFSNPSSECSMKEGIQTCMF PKETDIKTSENTAEFKERELCPLKTSKKLPENHLPRNSPQYHQPDLPEISRKNNGNNQQ VPVKNEVDHCENLKKVDTKPSSEKKIHKTSREDMFSEKQDIPFVEQEDPYRKKKLQEKR **EGNLQNLNWSKSRTCRKNKKRGVAPVSRPPEQSDLKLVCSDFERSELSSDINVRSWCI QESTREVCKADAEIASSLPAAQREAEGYYQKPEKKCVDKFCSDSSSDCGSSSGSVRAS** RGSWGSWSSTSSSDGDKKPMVDAQHFLPAGDSVSQNDFPSEAPISLNLSHNICNPMT VNSLPQYAEPSCPSLPAGPTGVEEDKGLYSPGDLWPTPPVCVTSSLNCTLENGVPCVI QESAPVHNSFIDWSATCEGQFSSAYCPLELNDYNAFPEENMNYANGFPCPADVQTDFI DHNSQSTWNTPPNMPAAWGHASFISSPPYLTSTRSLSPMSGLFGSIWAPQSDVYENC CPINPTTEHSTHMENQAVVCKEYYPGFNPFRAYMNLDIWTTTANRNANFPLSRDSSYC **GNV**

SEQID No:203

ASGEWRVSGGRPAGAGRPEEALAAGSDPRGAAARLACSAPTPGGGTMPFDFRRFDIY RKVPKDLTQPTYTGAIISICCCLFILFLFLSELTGFITTEVVNELYVDDPDKDSGGKIDVSL NISLPNLHCELVGLDIQDEMGRHEVGHIDNSMKIPLNNGAGCRFEGQFSINKVPGNFHV STHSATAQPQNPDMTHVIHKLSFGDTLQVQNIHGAFNALGGADRLTSNPLASHDYILKIV PTVYEDKSGKQRYSYQYTVANKEYVAYSHTGRIIPAIWFRYDLSPITVKYTERRQPLYRFITTICAIIGGTFTVAGILDSCIFTASEAWKKIQLGKMH

SEQID No:204

NSKKMQSWYSMLSPTYKQRNEDFRKLFSKLPEAERLIVDYSCALQREILLQGRLYLSEN WICFYSNIFRWETTISIQLKEVTCLKKEKTAKLIPNAIQICTESEKHFFTSFGARDRCFLLIF RLWQNALLEKTLSPRELWHLVHQCYGSELGLTSEDEDYVSPLQLNGLGTPKEVGDVIA

LSDITSSGAADRSQEPSPVGSRRGHVTPNLSRASSDADHGAEEDKEEQVDSQPDASS SQTVTPVAEPPSTEPTQPDGPTTLGPLDLLPSEELLTDTSNSSSSTGEEADLAALLPDLS -GRLLINSVFHVGAERLQQMLFSDSPFLQGFLQQCKFTDVTLSPWSGDSKCHQRRVLTY TIPISNPLGPKSASVVETQTLFRRGPQAGGCVVDSEVLTQGIPYQDYFYTAHRYCILGLA RNKARLRVSSEIRYRKQPWSLVKSLIEKNSWSGIEDYFHHLERELAKAEKLSLEEGGKD ARGLLSGLRRRKRPLSWRAHGDGPQHPDPDPCARAGIHTSGSLSSRFSEPSVDQGPG AGIPSALVLISIVSLIILIALNVLLFYRLWSLERTAHTFESWHSLALAKGKFPQTATEWAEIL _ALQKQFHSVEVHKWRQILRASVELLDEMKFSLEKLHQGITVSDPPFDTQPRPDDSFS

SEQID No:205

MLGLLVALLALGLAVFALLDVWYLVRLPCAVLRARLLQPRVRDLLAEQRFPGRVLPSDL DLLLHMNNARYLREADFARVAHLTRCGVLGALRELRAHTVLAASCARHRRSLRLLEPFE VRTRLLGWDDRAFYLEARFVSLRDGFVCALLRFRQHLLGTSPERVVQHLCQRRVEPPE LPADLQHWISYNEASSQLLRMESGLSDVTKDQ

SEQID No:206

MTLARFVLALMLGALPEVVGFDSVLNDSLHHSHRHSPPAGPHYPYYLPTQQRPPTTRP PPPLPRFPRPPRALPAQRPHALQAGHTPRPHPWGCPAGEPWVSVTDFGAPCLRWAE VPPFLERSPPASWAQLRGQRHNFCRSPDGAGRPWCFYGDARGKVDWGYCDCRHGS VRLRGGKNEFEGTVEVYASGVWGTVCSSHWDDSDASVICHQLQLGGKGIAKQTPFSG LGLIPIYWSNVRCRGDEENILLCEKDIWQGGVCPQKMAAAVTCSFSHGPTFPIIRLAGGS SVHEGRVELYHAGQWGTVCDDQWDDADAEVICRQLGLSGIAKAWHQAYFGEGSGPV MLDEVRCTGNELSIEQCPKSSWGEHNCGHKEDAGVSCTPLTDGVIRLAGGKGSHEGR LEVYYRGQWGTVCDDGWTELNTYVVCRQLGFKYGKQASANHFEESTGPIWLDDVSCS GKETRFLQCSRRQWGRHDCSHREDVSIACYPGGEGHRLSLGFPVRLMDGENKKEGR VEVFINGQWGTICDDGWTDKDAAVICRQLGYKGPARARTMAYFGEGKGPIHVDNVKCT GNERSLADCIKQDIGRHNCRHSEDAGVICDYFGKKASGNSNKESLSSVCGLRLLHRRQ KRIIGGKNSLRGGWPWQVSLRLKSSHGDGRLLCGATLLSSCWVLTAAHCFKRYGNSTR SYAVRYGDYHTLVPEEFEEEIGVQQIVIHREYRPDRSDYDIALVRLQGPEEQCARFSSH VLPACLPLWRERPQKTASNCYITGWGDTGRAYSRTLQQAAIPLLPKRFCEERYKGRFT GRMLCAGNLHEHKRVDSCQGDSGGPLMCERPGESWVVYGVTSWGYGCGVKDSPGV YTKVSAFVPWIKSVTKL

MEDGGLTAFEEDQRCLSQSLPLPVSAEGPAAQTTAEPSRSFSSAHRHLSRRNGLSRLC QSRTALSEDRWSSYCLSSLAAQNICTSKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSS GWSSPLLPAPVCNPNKAIFTVDAKTTEILVANDKACGLLGYSSQDLIGQKLTQFFLRSDS DVVEALSEEHMEADGHAAVVFGTVVDIISRSGEKIPVSVWMKRMRQERRLCCVVVLEP VERVSTWVAFQSDGTVTSCDSLFAHLHGYVSGEDVAGQHITDLIPSVQLPPSGQHIPKN LKIQRSVGRARDGTTFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLP DGTIHGINHSFALTLFGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNE SGCGERTLDPWQGQDPAEGGQDPRINVVLAGGHVVPRDEIRKLMESQDIFTGTQTELI AGGQLLSCLSPQPAPGVDNVPEGSLPVHGEQALPKDQQITALGREEPVAIESPGQDLL GESRSEPVDVKPFASCEDSEAPVPAEDGGSDAGMCGLCQKAQLERMGVSGPSGSDL WAGAAVAKPQAKGQLAGGSLLMHCPCYGSEWGLWWRSQDLAPSPSGMAGLSFGTP TLDEPWLGVENDREELQTCLIKEQLSQLSLAGALDVPHAELVPTECQAVTAPVSSCDLG GRDLCGGCTGSSSACYALATDLPGGLEAVEAQEVDVNSFSWNLKELFFSDQTDQTSS NCSCATSELRETPSSLAVGSDPDVGSLQEQGSCVLDDRELLLLTGTCVDLGQGRRFRE SCVGHDPTEPLEVCLVSSEHYAASDRESPGHVPSTLDAGPEDTCPSAEEPRLNVQVTS TPVIVMRGAAGLQREIQEGAYSGSCHHRDGLRLSIQFEVRRVELQGPTPLFCCWLVKD LLHSQRDSAARTRLFLASLPGSTHSTAAELTGPSLVEVLRARPWFEEPPKAVELEGLAA CEGEYSQKYSTMSPLGSGAFGFVWTAVDKEKNKEVVVKFIKKEKVLEDCWIEDPKLGK VTLEIAILSRVEHANIIKVLDIFENQGFFQLVMEKHGSGLDLFAFIDRHPRLDEPLASYIFR QLVSAVGYLRLKDIIHRDIKDENIVIAEDFTIKLIDFGSAAYLERGKLFYTFCGTIEYCAPEV LMGNPYRGPELEMWSLGVTLYTLVFEENPFCELEETVEAAIHPPYLVSKELMSLVSGLL QPVPERRTTLEKLVTDPWVTQPVNLADYTWEEVCRVNKPESGVLSAASLEMGNRSLS DVAQAQELCGGPVPGEAPNGQGCLHPGDPRLLTS

SEQID No:208

MEPGTGGSRKRLGPRAGFRFWPPFFPRRSQAGSSKFPTPLGPENSGNPTLLSSAQPE TRVSYWTKLLSQLLAPLPGLLQKVLIWSQLFGGMFPTRWLDFAGVYSALRALKGREKP AAPTAQKSLSSLQLDSSDPSVTSPLDWLEEGIHWQYSPPDLKLELKAKGSALDPAAQAF LLEQQLWGVELLPSSLQSRLYSNRELGSSPSGPLNIQRIDDFSVVSYLLNPSYLDCFPRL EVSYQNSDGNSEVVGFQTLTPESSCLREDHCHPQPLSAELIPASWQGCPPLSTEGLPEI HHLRMKRLEFLQQASKGQDLPTPDQDNGYHSLEEEHSLLRMDPKHCRDNPTQFVPAA GDIPGNTQESTEEKIELLTTEVPLALEEESPSEGCPSSEIPMEKEPGEGRISVVDYSYLE GDLPISARPACSNKLIDYILGGASSDLETSSDPEGEDWDEEAEDDGFDSDSSLSDSDLE

QDPEGLHLWNSFCSVDPYNPQNFTATIQTAARIVPEEPSDSEKDLSGKSDLENSSQSG SLPETPEHSSGEEDDWESSADEAESLKLWNSFCNSDDPYNPLNFKAPFQTSGENEKG CRDSKTPSESIVAISECHTLLSCKVQLLGSQESECPDSVQRDVLSGGRHTHVKRKKVTF LEEVTEYYISGDEDRKGPWEEFARDGCRFQKRIQETEDAIGYCLTFEHRERMFNRLQG TCFKGLNVLKQC

SEQID No:209

MNLERVSNEEKLNLCRKYYLGGFAFLPFLWLVNIFWFFREAFLVPAYTEQSQIKGYVWR SAVGFLFWVIVLTSWITIFQIYRPRWGALGDYLSFTIPLGTP

SEQID No:210

MTELPAPLSYFQNAQMSEDNHLSNTNDNRERQEHNDRRSLGHPEPLSNGRPQGNSR QVVEQDEEEDEELTLKYGAKHVIMLFVPVTLCMVVVVATIKSVSFYTRKDGQLIYTPFTE DTETVGQRALHSILNAAIMISVIVVMTILLVVLYKYRCYKVIHAWLIISSLLLLFFFSFIYLGE VFKTYNVAVDYITVALLIWNLGVVGMISIHWKGPLRLQQAYLIMISALMALVFIKYLPEWT AWLILAVISVYDLVAVLCPKGPLRMLVETAQERNETLFPALIYSSTMVWLVNMAEGDPEA QRRVSKNSKYNAESTERESQDTVAENDDGGFSEEWEAQRDSHLGPHRSTPESRAAV QELSSSILAGEDPEERGVKLGLGDFIFYSVLVGKASATASGDWNTTIACFVAILIGLCLTL LLLAIFKKALPALPISITFGLVFYFATDYLVQPFMDQLAFHQFYI

SEQID No:211

MAAETILSSLIGILLIGILIPASITGGVGSLNIEELSEMRYGIEILPLPVMGGQSQSSDV VIVSSKYKQRYECRLPAGAIHFQREREEETPAYQGPGIPELISPMRDAPCLIKTKDWWT YEFCYGRHIQQYHMEDSEIKGEVLYLGYYQSAFDWDDETAKASKQHRLKRYHSQTYG NGSKCDLNGRPREAEVRFLCDEGAGISGDYIDRVDEPLSCSYVLTIRTPRLCPHPLLRP PPSAAPQAILCHPSLQPEEYMAYVQRQADSKQYGDKIIEELQDLGPQVWSETKSGVAP QKMAGASPTKDDSKDSDFWKMLNEPEDQAPGGEEVPAEEQDPSPEAADSASGAPND FQNNVQVKVIRSPADLIRFIEELKGGTKKGKPNIGQEQPVDDAAEVPQREPEKERGDPE RQREMEEEEDEDEDEDEDEDERQLLGEFEKELEGILLPSDRDRLRSEVKAGMERELEN IIQETEKELDPDGLKKESERDRAMLALTSTLNKLIKRLEEKQSPELVKKHKKKRVVPKKP PPSPQPTEEDPEHRVRVRVTKLRLGGPNQDLTVLEMKRENPQLKQIEGLVKELLEREG LTAAGKIEIKIVRPWAEGTEEGARWLTDEDTRNLKEIFFNILVPGAEEAQKERQRQKELE SNYRRVWGSPGGEGTGDLDEFDF

MAVVPLLLLGGLWSAVGASSLGVVTCGSVVKLLNTRHNVRLHSHDVRYGSGSGQQSV TGVTSVDDSNSYWRIRGKSATVCERGTPIKCGQPIRLTHVNTGRNLHSHHFTSPLSGN QEVSAFGEEGEGDYLDDWTVLCNGPYWVRDGEVRFKHSSTEVLLSVTGEQYGRPISG QKEVHGMAQPSQNNYWKAMEGIFMKPSELLKAEAHHAEL

SEQID No:213

MEASGKLICRQRQVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQRE FSRRGVRVVSRGNKLHLQLTQETADLLLNEKLDREDLCGHTEPCVLRFQVLLESPFEFF QAELQVIDINDHSPVFLDKQMLVKVSESSPPGTAFPLKNAEDLDIGQNNIENYIISPNSYF RVLTRKRSDGRKYPELVLDNALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVVDVND NAPEFQQPFYRVQISEDSPISFLVVKVSATDVDTGVNGEISYSLFQASDEISKTFKVDFLT GEIRLKKQLDFEKFQSYEVNIEARDAGGFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPE NAPETVVALFSVSDLDSGENGKISCSIQEDLPFLLKSSVGNFYTLLTETPLDRESRAEYN VTITVTDLGTPRLTTHLNMTVLVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDR DSGTNAQVTYSLLPPQDPHLPLASLVSINTDNGHLFALRSLDYEALQAFEFRVGASDRG SPALSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDS GQNAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPCS ATATLHLLLVDGFSQPYLPLPEAAPAQGQADSLTVYLVVALASVSSLFLFSVLLFVAVLLC RRSRAASVGRCSVPEGPFPGHLVDVRGTGSLSQNYQYEVCLAGGSGTNEFQFLKPVL PNIQGHSFGPEMEQNSNFRNGFGFSLQLK

SEQID No:214

MASRGVVGIFFLSAVPLVCLELRRGIPDIGIKDFLLLCGRILLLLALLTLIISVTTSWLNSFKS PQVYLKEEEEKNEKRQKLVRKKQQEAQGEKASRYIENVLKPHQEMKLRKLEERFYQMT GEAWKLSSGHKLGGDEGTSQTSFETSNREAAKSQNLPKPLTEFPSPAEQPTCKEIPDL PEEPSQTAEEVVTVALRCPSGNVLRRRFLKSYSSQVLFDWMTRIGYHISLYSLSTSFPR RPLAVEGGQSLEDIGITVDTVLILEEKEQTN

SEQID No:215

MAAAEEEDGGPEGPNRERGGAGATFECNICLETAREAVVSVCGHLYCWPCLHQWLET RPERQECPVCKAGISREKVVPLYGRGSQKPQDPRLKTPPRPQGQRPAPESRGGFQPF GDTGGFHFSFGVGAFPFGFFTTVFNAHEPFRRGTGVDLGQGHPASSWQDSLFLFLAIF FFFWLLSI

MKFLLDILLLPLLIVCSLESFVKLFIPKRRKSVTGEIVLITGAGHGIGRLTAYEFAKLKSKL VLWDINKHGLEETAAKCKGLGAKVHTFVVDCSNREDIYSSAKKVKAEIGDVSILVNNAGV VYTSDLFATQDPQIEKTFEVNVLAHFWTTKAFLPAMTKNNHGHIVTVASAAGHVSVPFLL AYCSSKFAAVGFHKTLTDELAALQITGVKTTCLCPNFVNTGFIKNPSTSLGPTLEPEEVV NRLMHGILTEQKMIFIPSSIAFLTTLERILPERFLAVLKRKISVKFDAVIGYKMKAQ

SEQID No:217

MWSAGRGGAAWPVLLGLLLALLVPGGGAAKTGAELVTCGSVLKLLNTHHRVRLHSHDI KYGSGSGQQSVTGVEASDDANSYWRIRGGSEGGCPCGSPVRCGQAVRLTHVLTGKN LHTHHFPSPLSNNQEVSAFGEDGEGDDLDLWTVRCSGQHWEREAAVRLQHVGTSVFL SVTGEQYGSPIRGQHEVHGMPSANTHNTWKAMEGIFIKPSVEPSAGHDEL

SEQID No:218

GRWASGEMAPSGSLAVPLAVLVLLLWGAPWTHGRRSNVRVITDENWRELLEGDWMIE FYAPWCPACQNLQPEWESFAEWGEDLEVNIAKVDVTEQPGLSGRFIITALPTIYHCKDG EFRRYQGPRTKKDFINFISDKEWKSIEPVSSWFGPGSVLMSSMSALFQLSMWIRTCHN YFIEDLGLPVWGSYTVFALATLFSGLLLGLCMIFVADCLCPSKRRRPQPYPYPSKKLLSE SAQPLKKVEEEQEADEEDVSEEEAESKEGTNKDFPQNAIRQRSLGPSLATDKS

SEQID No:219

HPAGLAAAAAGTPRLPSKRRIPVSQPGMADPHQLFDDTSSAQSRGYGAQRAPGGLSY PAASPTPHAAFLADPVSNMAMAYGSSLAAQGKELVDKNIDRFIPITKLKYYFAVDTMYV GRKLGLLFFPYLHQDWEVQYQQDTPVAPRFDVNAPDLYIPAMAFITYVLVAGLALGTQD RFSPDLLGLQASSALAWLTLEVLAILLSLYLVTVNTDLTTIDLVAFLGYKYVGMIGGVLMG LLFGKIGYYLVLGWCCVAIFVFMIRTLRLKILADAAAEGVPVRGARNQLRMYLTMAVAAA QPMLMYWLTFHLVR

SEQID No:220

MAATALLEAGLARVLFYPTLLYTLFRGKVPGRAHRDWYHRIDPTVLLGALPLRSLTRQLV QDENVRGVITMNEEYETRFLCNSSQEWKRLGVEQLRLSTVDMTGIPTLDNLQKGVQFA LKYQSLGQCVYVHCKAGRSRSATMVAAYLIQVHKWSPEEAVRAIAKIRSYIHIRPGQLDV LKEFHKQITARATKDGTFVISKT

MNTVLSRANSLFAFSLSVMAALTFGCFITTAFKDRSVPVRLHVSRIMLKNVEDFTGPRER SDLGFITSDITADLENIFDWNVKQLFLYLSAEYSTKNNALNQVVLWDKIVLRGDNPKLLLK DMKTKYFFFDDGNGLKGNRNVTLTLSWNVVPNAGILPLVTGSGHVSVPFPDTYEITKSY

SEQID No:222

MALRGFCSADGSDPLWDWNVTWNTSNPDFTKCFQNTVLVWVPCFYLWACFPFYFLYL SRHDRGYIQMTPLNKTKTALGFLLWIVCWADLFYSFWERSRGIFLAPVFLVSPTLLGITT LLATFLIQLERRKGVQSSGIMLTFWLVALVCALAILRSKIMTALKEDAQVDLFRDITFYVYF SLLLIQLVLSCFSDRSPLFSETIHDPNPCPESSASFLSRITFWWITGLIVRGYRQPLEGSD LWSLNKEDTSEQVVPVLVKNWKKECAKTRKQPVKVVYSSKDPAQPKESSKVDANEEV **EALIVKSPQKEWNPSLFKVLYKTFGPYFLMSFFFKAIHDLMMFSGPQILKLLIKFVNDTKA** PDWQGYFYTVLLFVTACLQTLVLHQYFHICFVSGMRIKTAVIGAVYRKALVITNSARKSS TVGEIVNLMSVDAQRFMDLATYINMIWSAPLQVILALYLLWLNLGPSVLAGVAVMVLMVP VNAVMAMKTKTYQVAHMKSKDNRIKLMNEILNGIKVLKLYAWELAFKDKVLAIRQEELKV LKKSAYLSAVGTFTWVCTPFLVALCTFAVYVTIDENNILDAQTAFVSLALFNILRFPLNILP MVISSIVQASVSLKRLRIFLSHEELEPDSIERRPVKDGGGTNSITVRNATFTWARSDPPTL NGITFSIPEGALVAVVGQVGCGKSSLLSALLAEMDKVEGHVAIKGVNLSGGQKQRVSLA RAVYSNADIYLFDDPLSAVDAHVGKHIFENVIGPKGMLKNKTRILVTHSMSYLPQVDVIIV MSGGKISEMGSYQELLARDGAFAEFLRTYASTEQEQDAEENGVTGVSGPGKEAKQME NGMLVTDSAGKQLQRQLSSSSSYSGDISRHHNSTAELQKAEAKKEETWKLMEADKAQ TGQVKLSVYWDYMKAIGLFISFLSIFLFMCNHVSALASNYWLSLWTDDPIVNGTQEHTK VRLSVYGALGISQGIAVFGYSMAVSIGGILASRCLHVDLLHSILRSPMSFFERTPSGNLVN RFSKELDTVDSMIPEVIKMFMGSLFNVIGACIVILLATPIAAIIIPPLGLIYFFVQRFYVASSR QLKRLESVSRSPVYSHFNETLLGVSVIRAFEEQERFIHQSDLKVDENQKAYYPSIVANR WLAVRLECVGNCIVLFAALFAVISRHSLSAGLVGLSVSYSLQVTTYLNWLVRMSSEMET NIVAVERLKEYSETEKEAPWQIQETAPPSSWPQVGRVEFRNYCLRYREDLDFVLRHINV TINGGEKVGIVGRTGAGKSSLTLGLFRINESAEGEIIIDGINIAKIGLHDLRFKITIIPQDPVLF SGSLRMNLDPFSQYSDEEVWTSLELAHLKDFVSALPDKLDHECAEGGENLSVGQRQLV CLARALLRKTKILVLDEATAAVDLETDDLIQSTIRTQFEDCTVLTIAHRLNTIMDYTRVIVLD KGEIQEYGAPSDLLQQRGLFYSMAKDAGLV

MARGKAKEEGSWKKFIWNSEKKEFLGRTGGSWFKILLFYVIFYGCLAGIFIGTIQVMLLTI SEFKPTYQDRVAPPGLTQIPQIQKTEISFRPNDPKSYEAYVLNIVRFLEKYKDSAQRDDM IFEDCGDVPSEPKERGDFNHERGERKVCRFKLEWLGNCSGLNDETYGYKEGKPCIIIKL NRVLGFKPKPPKNESLETYPVMKYNPNVLPVQCTGKRDEDKDKVGNVEYFGLGNSPG FPLQYYPYYGKLLQPKYLQPLLAVQFTNLTMDTEIRIECKAYGENIGYSEKDRFQGRFDV KIEVKS

SEQID No:224

MKVARFQKIPNGENETMIPVLTSKKASELPVSEVASILQADLQNGLNKCEVSHRRAFHG WNKFDISEDEPLWKKYISQFKNPLIMLLLASAVISVLMHQFDDAVSITVAILIVVTVAFVQE YRSEKSLEELSKLVPPECHCVREGKLEHTLARDLVPGDTVCLSVGDRVPADLRLFEAVD LSIDESSLTGETTPCSKVTAPQPAATNGDLASRSNIAFMGTLVRCGKAKGVVIGTGENS **EFGEVFKMMQAEEAPKTPLQKSMDLLGKQLSFYSFGIIGIIMLVGWLLGKDILEMFTISVS** LAVAAIPEGLPIVVTVTLALGVMRMVKKRAIVKKLPIVETLGCCNVICSDKTGTLTKNEMT VTHIFTSDGLHAEVTGVGYNQFGEVIVDGDVVHGFYNPAVSRIVEAGCVCNDAVIRNNT LMGKPTEGALIALAMKMGLDGLQQDYIRKAEYPFSSEQKWMAVKCVHRTQQDRPEICF MKGAYEQVIKYCTTYQSKGQTLTLTQQQRDVYQQEKARMGSAGLRVLALASGPELGQ LTFLGLVGIIDPPRTGVKEAVTTLIASGVSIKMITGDSQETAVAIASRLGLYSKTSQSVSGE EIDAMDVQQLSQIVPKVAVFYRASPRHKMKIIKSLQKNGSVVAMTGDGVNDAVALKAAD IGVAMGQTGTDVCKEAADMILVDDDFQTIMSAIEEGKGIYNNIKNFVRFQLSTSIAALTLIS LATLMNFPNPLNAMQILWINIIMDGPPAQSLGVEPVDKDVIRKPPRNWKDSILTKNLILKIL VSSIIIVCGTLFVFWRELRDNVITPRDTTMTFTCFVFFDMFNALSSRSQTKSVFEIGLCSN RMFCYAVLGSIMGQLLVIYFPPLQKVFQTESLSILDLLFLLGLTSSVCIVAEIIKKVERSRE KIOKHVSSTSSSFLEV

SEQID No:225

MAKNRRDRNSWGGFSEKTYEWSSEEEEPVKKAGPVQVLIVKDDHSFELDETALNRILL SEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVGDYNEPLTGFSWRG GSERETTGIQIWSEIFLINKPDGKKVAVLLMDTQGTFDSQSTLRDSATVFALSTMISSIQV YNLSQNVQEDDLQHLQLFTEYGRLAMEETFLKPFQSLIFLVRDWSFPYEFSYGADGGA KFLEKRLKVSGNQHEELQNVRKHIHSCFTNISCFLLPHPGLKVATNPNFDGKLKEIDDEFI KNLKILIPWLLSPESLDIKEINGNKITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANN LAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTKHLQLKEESVKLFRGVKKMGGEEFS

RRYLQQLESEIDELYIQYIKHNDSKNIFHAARTPATLFVVIFITYVIAGVTGFIGLDIIASLCN MIMGLTLITLCTWAYIRYSGEYRELGAVIDQVAAALWDQGSTNEALYKLYSAAATHRHLY HQAFPTPKSESTEQSEKKKM

SEQID No:226

MGCCSSASSAAQSSKREWKPLEDRSCTDIPWLLLFILFCIGMGFICGFSIATGAAARLVS
GYDSYGNICGQKNTKLEAIPNSGMDHTQRKYVFFLDPCNLDLINRKIKSVALCVAACPR
QELKTLSDVQKFAEINGSALCSYNLKPSEYTTSPKSSVLCPKLPVPASAPIPFFHRCAPV
NISCYAKFAEALITFVSDNSVLHRLISGVMTSKEIILGLCLLSLVLSMILMVIIRYISRVLVWIL
TILVILGSLGGTGVLWWLYAKQRRSPKETVTPEQLQIAEDNLRALLIYAISATVFTVILFLIM
LVMRKRVALTIALFHVAGKVFIHLPLLVFQPFWTFFALVLFWVYWIMTLLFLGTTGSPVQ
NEQGFVEFKISGPLQYMWWYHVVGLIWISEFILACQQMTVAGAVVTYYFTRDKRNLPFT
PILASVNRLIRYHLGTVAKGSFIITLVKIPRMILMYIHSQLKGKENACARCVLKSCICCLWC
LEKCLNYLNQNAYTATAINSTNFCTSAKDAFVILVENALRVATINTVGDFMLFLGKVLIVC
STGLAGIMLLNYQQDYTVWVLPLIIVCLFAFLVAHCFLSIYEMVVDVLFLCFAIDTKYNDG
SPGREFYMDKVLMEFVENSRKAMKEAGKGGVADSRELKPMLKKR

SEQID No:227

EKSGGPGTRERERKREERQSAWGRKERGREGWVRRRERSAANPRRRAWSPSQNS SPSRSRSQGGGCRDRQPCMMHLRLFCILLAAVSGAEGWGYYGCDEELVGPLYARSLG ASSYYSLLTAPRFARLHGISGWSPRIGDPNPWLQIDLMKKHRIRAVATQGSFNSWDWV TRYMLLYGDRVDSWTPFYQRGHNSTFFGNVNESAVVRHDLHFHFTARYIRIVPLAWNP RGKIGLRLGLYGCPYKADILYFDGDDAISYRFPRGVSRSLWDVFAFSFKTEEKDGLLLHA EGAQGDYVTLELEGAHLLLHMSLGSSPIQPRPGHTTVSAGGVLNDQHWHYVRVDRFG RDVNFTLDGYVQRFILNGDFERLNLDTEMFIGGLVGAARKNLAYRHNFRGCIENVIFNRV NIADLAVRRHSRITFEGKVAFRCLDPVPHPINFGGPHNFVQVPGFPRRGRLAVSFRFRT WDLTGLLLFSRLGDGLGHVELTLSEGQVNVSIAQSGRKKLQFAAGYRLNDGFWHEVNF VAQENHAVISIDDVEGAEVRVSYPLLIRTGTSYFFGGCPKPASRWDCHSNQTAFHGCM ELLKVDGQLVNLTLVEGRRLGFYAEVLFDTCGITDRCSPNMCEHDGRCYQSWDDFICY CELTGYKGETCHTPLYKESCEAYRLSGKTSGNFTIDPDGSGPLKPFVVYCDIRENRAWT VVRHDRLWTTRVTGSSMERPFLGAIQYWNASWEEVSALANASQHCEQWIEFSCYNSR LLNTAGGYPYSFWIGRNEEQHFYWGGSQPGIQRCACGLDRSCVDPALYCNCDADQPQ WRTDKGLLTFVDHLPVTQVVIGDTNRSTSEAQFFLRPLRCYGDRNSWNTISFHTGAALR FPPIRANHSLDVSFYFRTSAPSGVFLENMGGPYCQWRRPYVRVELNTSRDVVFAFDVG

NGDENLTVHSDDFEFNDDEWHLVRAEINVKQARLRVDHRPWVLRPMPLQTYIWMEYD QPLYVGSAELKRRPFVGCLRAMRLNGVTLNLEGRANASEGTSPNCTGHCAHPRLPCF HGGRCVERYSYYTCDCDLTAFDGPYCNHDIGGFFEPGTWMRYNLQSALRSAAREFSH MLSRPVPGYEPGYIPGYDTPGYVPGYHGPGYRLPDYPRPGRPVPGYRGPVYNVTGEE VSFSFSTSSAPAVLLYVSSFVRDYMAVLIKDDGTLQLRYQLGTSPYVYQLTTRPVTDGQ PHSINITRVYRNLFIQVDYFPLTEQKFSLLVDSQLDSPKALYLGRVMETGVIDPEIQRYNT PGFSGCLSGVRFNNVAPLKTHFRTPRPMTAELAEALRVQGELSESNCGAMPRLVSEVP PELDPWYLPPDFPYYHDEGWVAILLGFLVAFLLLGLVGMLVLFYLQNHRYKGSYHTNEP KAAHEYHPGSKPPLPTSGPAQVPTPTAAPNQAPASAPAPAPTPAPAPGPRDQNLPQIL EESRSE

SEQID No:228

MGNRGMEDLIPLVNRLQDAFSAIGQNADLDLPQIAVVGGQSAGKSSVLENFVGRDFLP
RGSGIVTRRPLVLQLVNATTEYAEFLHCKGKKFTDFEEVRLEIEAETDRVTGTNKGISPV
PINLRVYSPHVLNLTLVDLPGMTKVPVGDQPPDIEFQIRDMLMQFVTKENCLILAVSPAN
SDLANSDALKVAKEVDPQGQRTIGVITKLDLMDEGTDARDVLENKLLPLRRGYIGVVNR
SQKDIDGKKDITAALAAERKFFLSHPSYRHLADRMGTPYLQKVLNQQLTNHIRDTLPGLR
NKLQSQLLSIEKEVEEYKNFRPDDPARKTKALLQMVQQFAVDFEKRIEGSGDQIDTYEL
SGGARINRIFHERFPFELVKMEFDEKELRREISYAIKNIHGIRTGLFTPDMAFETIVKKQVK
KIREPCLKCVDMVISELISTVRQCTKKLQQYPRLREEMERIVTTHIREREGRTKEQVMLLI
DIELAYMNTNHEDFIGFANAQQRSNQMNKKKTSGNQDEILVIRKGWLTINNIGIMKGGSK
EYWFVLTAENLSWYKDDEEKEKKYMLSVDNLKLRDVEKGFMSSKHIFALFNTEQRNVY
KDYRQLELACETQEEVDSWKASFLRAGVYPERVGDKEKASETEENGSDSFMHSMDPQ
LERQVETIRNLVDSYMAIVNKTVRDLMPKTIMHLMINNTKEFIFSELLANLYSCGDQNTLM
EESAEQAQRRDEMLRMYHALKEALSIIGNINTTTVSTPMPPPVDDSWLQVQSVPAGRR
SPTSSPTPQRRAPAVPPARPGSRGPAPGPPPAGSALGGAPPVPSRPGASPDPFGPPP
QVPSRPNRAPPGVPSRSGQASPSRPESPRPPFDL

SEQID No:229

MAARRQGPARSANPRPQFPGVCGREHAATLRAPGRGGGASPAQIGTRGRGGHNFAP NLTARSAVTSGLGGPPAAVMVGSLNCIVAVSQNMGIGKNGDLPWPPLRNEFRYFQRM TTTSSVEGKQNLVIMGKKTWFSIPEKNRPLKGRINLVLSRELKEPPQGAHFLSRSLDDAL KLTEQPELANKVDMVWIVGGSSVYKEAMNHPGHLKLFVTRIMQDFESDTFFPEIDLEKY KLLPEYPGVLSDVQEEKGIKYKFEVYEKND

MDRGTLPLAVALLLASCSLSPTSLAETVHCDLQPVGPERGEVTYTTSQVSKGCVAQAP
NAILEVHVLFLEFPTGPSQLELTLQASKQNGTWPREVLLVLSVNSSVFLHLQALGIPLHL
AYNSSLVTFQEPPGVNTTELPSFPKTQILEWAAERGPITSAAELNDPQSILLRLGQAQGS
LSFCMLEASQDMGRTLEWRPRTPALVRGCHLEGVAGHKEAHILRVLPGHSAGPRTVTV
KVELSCAPGDLDAVLILQGPPYVSWLIDANHNMQIWTTGEYSFKIFPEKNIRGFKLPDTP
QGLLGEARMLNASIVASFVELPLASIVSLHASSCGGRLQTSPAPIQTTPPKDTCSPELLM
SLIQTKCADDAMTLVLKKELVAHLKCTITGLTFWDPSCEAEDRGDKFVLRSAYSSCGMQ
VSASMISNEAVVNILSSSSPQRKKVHCLNMDSLSFQLGLYLSPHFLQASNTIEPGQQSF
VQVRVSPSVSEFLLQLDSCHLDLGPEGGTVELIQGRAAKGNCVSLLSPSPEGDPRFSFL
LHFYTVPIPKTGTLSCTVALRPKTGSQDQEVHRTVFMRLNIISPDLSGCTSKGLVLPAVL
GITFGAFLIGALLTAALWYIYSHTRSPSKREPVVAVAAPASSESSSTNHSIGSTQSTPCST
SSMA

SEQID No:231

MCASVKYNIRGPALIPRMKTKHRIYYITLFSIVLLGLIATGMFQFWPHSIESSNDWNVEKR SIRDVPVVRLPADSPIPERGDLSCRMHTCFDVYRCGFNPKNKIKVYIYALKKYVDDFGVS VSNTISREYNELLMAISDSDYYTDDINRACLFVPSIDVLNQNTLRIKETAQAMAQLSRWD RGTNHLLFNMLPGGPPDYNTALDVPRDRALLAGGGFSTWTYRQGYDVSIPVYSPLSAE VDLPEKGPGPRQYFLLSSQVGLHPEYREDLEALQVKHGESVLVLDKCTNLSEGVLSVR KRCHKHQVFDYPQVLQEATFCVVLRGARLGQAVLSDVLQAGCVPVVIADSYILPFSEVL DWKRASVVVPEEKMSDVYSILQSIPQRQIEEMQRQARWFWEAYFQSIKAIALATLQIIND RIYPYAAISYEEWNDPPAVKWGSVSNPLFLPLIPPQSQGFTAIVLTYDRVESLFRVITEVS KVPSLSKLLVVWNNQNKNPPEDSLWPKIRVPLKVVRTAENKLSNRFFPYDEIETEAVLAI DDDIIMLTSDELQFGYEVWREFPDRLVGYPGRLHLWDHEMNKWKYESEWTNEVSMVL TGAAFYHKYFNYLYTYKMPGDIKNWVDAHMNCEDIAMNFLVANVTGKAVIKVTPRKKFK CPECTAIDGLSLDQTHMVERSECINKFASVFGTMPLKVVEHRADPVLYKDDFPEKLKSF PNIGSL

SEQID No:232

.

MTGYTMLRNGGAGNGGQTCMLRWSNRIRLTWLSFTLFVILVFFPLIAHYYLTTLDEADE AGKRIFGPRVGNELCEVKHVLDLCRIRESVSEELLQLEAKRQELNSEIAKLNLKIEACKKS IENAKQDLLQLKNVISQTEHSYKELMAQNQPKLSLPIRLLPEKDDAGLPPPKATRGCRLH

NCFDYSRCPLTSGFPVYVYDSDQFVFGSYLDPLVKQAFQATARANVYVTENADIACLYV
ILVGEMQEPVVLRPAELEKQLYSLPHWRTDGHNHVIINLSRKSDTQNLLYNVSTGRAMV
AQSTFYTVQYRPGFDLVVSPLVHAMSEPNFMEIPPQVPVKRKYLFTFQGEKIESLRSSL
QEARSFEEEMEGDPPADYDDRIIATLKAVQDSKLDQVLVEFTCKNQPKPSLPTEWALC
GEREDRLELLKLSTFALIITPGDPRLVISSGCATRLFEALEVGAVPVVLGEQVQLPYQDM
LQWNEAALVVPKPRVTEVHFLLRSLSDSDLLAMRRQGRFLWETYFSTADSIFNTVLAMI
RTRIQIPAAPIREEAAAEIPHRSGKAAGTDPNMADNGDLDLGPVETEPPYASPRYLRNFT
LTVTDFYRSWNCAPGPFHLFPHTPFDPVLPSEAKFLGSGTGFRPIGGGAGGSGKEFQA
ALGGNVPREQFTVVMLTYEREEVLMNSLERLNGLPYLNKVVVVWNSPKLPSEDLLWPD
IGVPIMVVRTEKNSLNNRFLPWNEIETEAILSIDDDAHLRHDEIMFGFRVWREARDRIVGF
PGRYHAWDIPHQSWLYNSNYSCELSMVLTGAAFFHKYYAYLYSYVMPQAIRDMVDEYI
NCEDIAMNFLVSHITRKPPIKVTSRWTFRCPGCPQALSHDDSHFHERHKCINFFVKVYG
YMPLLYTQFRVDSVLFKTRLPHDKTKCFKFI

SEQID No:233

MGPGRPAPAPWPRHLLRCVLLLGCLHLGRPGAPGDAALPEPNVFLIFSHGLQGCLEAQ GGQVRVTPACNTSLPAQRWKWVSRNRLFNLGTMQCLGTGWPGTNTTASLGMYECDR EALNLRWHCRTLGDQLSLLLGARTSNISKPGTLERGDQTRSGQWRIYGSEEDLCALPY HEVYTIQGNSHGKPCTIPFKYDNQWFHGCTSTGREDGHLWCATTQDYGKDERWGFC PIKSNDCETFWDKDQLTDSCYQFNFQSTLSWREAWASCEQQGADLLSITEIHEQTYING LLTGYSSTLWIGLNDLDTSGGWQWSDNSPLKYLNWESDQPDNPSEENCGVIRTESSG GWQNRDCSIALPYVCKKKPNATAEPTPPDRWANVKVECEPSWQPFQGHCYRLQAEK RSWQESKKACLRGGGDLVSIHSMAELEFITKQIKQEVEELWIGLNDLKLQMNFEWSDG SLVSFTHWHPFEPNNFRDSLEDCVTIWGPEGRWNDSPCNQSLPSICKKAGQLSQGAA **EEDHGCRKGWTWHSPSCYWLGEDQVTYSEARRLCTDHGSQLVTITNRFEQAFVSSLI** YNWEGEYFWTALQDLNSTGSFFWLSGDEVMYTHWNRDQPGYSRGGCVALATGSAM GLWEVKNCTSFRARYICRQSLGTPVTPELPGPDPTPSLTGSCPQGWASDTKLRYCYKV **FSSERLQDKKSWVQAQGACQELGAQLLSLASYEEEHFVANMLNKIFGESEPEIHEQHW FWIGLNRRDPRGGQSWRWSDGVGFSYHNFDRSRHDDDDIRGCAVLDLASLQWVAMQ** CDTQLDWICKIPRGTDVREPDDSPQGRREWLRFQEAEYKFFEHHSTWAQAQRICTWF QAELTSVHSQAELDFLSHNLQKFSRAQEQHWWIGLHTSESDGRFRWTDGSIINFISWA PGKPRPVGKDKKCVYMTASREDWGDQRCLTALPYICKRSNVTKETQPPDLPTTALGG CPSDWIQFLNKCFQVQGQEPQSRVKWSEAQFSCEQQEAQLVTITNPLEQAFITASLPN VTFDLWIGLHASQRDFQWVEQEPLMYANWAPGEPSGPSPAPSGNKPTSCAVVLHSPS

AHFTGRWDDRSCTEETHGFICQKGTDPSLSPSPAALPPAPGTELSYLNGTFRLLQKPLR WHDALLLCESHNASLAYVPDPYTQAFLTQAARGLRTPLWIGLAGEEGSRRYSWVSEEP LNYVGWQDGEPQQPGGCTYVDVDGAWRTTSCDTKLQGAVCGVSSGPPPPRRISYHG SCPQGLADSAWIPFREHCYSFHMELLLGHKEARQRCQRAGGAVLSILDEMENVFVWE HLQSYEGQSRGAWLGMNFNPKGGTLVWQDNTAVNYSNWGPPGLGPSMLSHNSCYW IQSNSGLWRPGACTNITMGVVCKLPRAEQSSFSPSALPENPAALVVVLMAVLLLLALLTA ALILYRRQSIERGAFEGARYSRSSSSPTEATEKNILVSDMEMNEQQE

SEQID No:234

MEDHQHVPIDIQTSKLLDWLVDRRHCSLKWQSLVLTIREKINAAIQDMPESEEIAQLLSG SYIHYFHCLRILDLLKGTEASTKNIFGRYSSQRMKDWQEIIALYEKDNTYLVELSSLLVRN VNYEIPSLKKQIAKCQQLQQEYSRKEEECQAGAAEMREQFYHSCKQYGITGENVRGEL LALVKDLPSQLAEIGAAAQQSLGEAIDVYQASVGFVCESPTEQVLPMLRFVQKRGNSTV YEWRTGTEPSVVERPHLEELPEQVAEDAIDWGDFGVEAVSEGTDSGISAEAAGIDWGI FPESDSKDPGGDGIDWGDDAVALQITVLEAGTQAPEGVARGPDALTLLEYTETRNQFL DELMELEIFLAQRAVELSEEADVLSVSQFQLAPAILQGQTKEKMVTMVSVLEDLIGKLTS LQLQHLFMILASPRYVDRVTEFLQQKLKQSQLLALKKELMVQKQQEALEEQAALEPKLD LLLEKTKELQKLIEADISKRYSGRPVNLMGTSL

SEQID No:235

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLS ELPSNLSVFTSYLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVL MLQNNQLRHVPTEALQNLRSLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIP VQAFRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLET LDLNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKAFVGNPSLITIHFYDNPIQFVGRSA FQHLPELRTLTLNGASQITEFPDLTGTANLESLTLTGAQISSLPQTVCNQLPNLQVLDLSY NLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRSLNLAWNKIAIIHPNAFSTLPS LIKLDLSSNLLSSFPITGLHGLTHLKLTGNHALQSLISSENFPELKVIEMPYAYQCCAFGV CENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLLDFEEDLKALHSVQC SPSPGPFKPCEHLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYISPIKLLIGVIAAVN MLTGVSSAVLAGVDAFTFGSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAALER GFSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLLGGSKYGASPLCLPLPFGEPSTM GYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNCPVAF

LSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYILFNPHFKEDLVSLRKQTYVWTRSKHP SLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSPAYPVTESCHLSSVAFVPCL

SEQID No:236

MIASHLLAYFFTELNHDQVQKVDQYLYHMRLSDETLLEISKRFRKEMEKGLGATTHPTA AVKMLPTFVRSTPDGTEHGEFLALDLGGTNFRVLWVKVTDNGLQKVEMENQIYAIPEDI MRGSGTQLFDHIAECLANFMDKLQIKDKKLPLGFTFSFPCHQTKLDESFLVSWTKGFKS SGVEGRDVVALIRKAIQRRGDFDIDIVAVVNDTVGTMMTCGYDDHNCEIGLIVGTGSNA CYMEEMRHIDMVEGDEGRMCINMEWGAFGDDGSLNDIRTEFDQEIDMGSLNPGKQLF EKMISGMYMGELVRLILVKMAKEELLFGGKLSPELLNTGRFETKDISDIEGEKDGIRKAR **EVLMRLGLDPTQEDCVATHRICQIVSTRSASLCAATLAAVLQRIKENKGEERLRSTIGVD** GSVYKKHPHFAKRLHKTVRRLVPGCDVRFLRSEDGSGKGAAMVTAVAYRLADQHRAR QKTLEHLQLSHDQLLEVKRRMKVEMERGLSKETHASAPVKMLPTYVCATPDGTEKGDF LALDLGGTNFRVLLVRVRNGKWGGVEMHNKIYAIPQEVMHGTGDELFDHIVQCIADFLE YMGMKGVSLPLGFTFSFPCQQNSLDESILLKWTKGFKASGCEGEDVVTLLKEAIHRREE **FDLDVVAVVNDTVGTMMTCGFEDPHCEVGLIVGTGSNACYMEEMRNVELVEGEEGRM** CVNMEWGAFGDNGCLDDFRTEFDVAVDELSLNPGKQRFEKMISGMYLGEIVRNILIDFT KRGLLFRGRISERLKTRGIFETKFLSQIESDCLALLQVRATLQHLGLESTCDDSIIVKEVCT VVARRAAQLCGAGMAAVVDRIRENRGLDALKVTVGVDGTLYKLHPHFAKVMHETVKDL **APKCDVSFLQSEDGSGKGAALITAVACRIREAGQR**

SEQID No:237

CDGQPDCADGSDEWDCSYVLPRKVITAAVIGSLVCGLLLVIALGCTCKLYAIRTQEYSIF APLSRMEAEIVQQQAPPSYGQLIAQGAIPPVEDFPTENPNDNSVLGNLRSLLQILRQDM TPGGGPGARRQRGRLMRRLVHRLRRWGLLPRTNTPARASEARSQVTPSAAPLEALD GGTGPAREGGAVGGQDGEQAPPLPIKAPLPSASTSPAPTTVPEAPGPLPSLPLEPSLLS GVVQALRGRLLPSLGPPGPTRSPPGPHTAVLALEDEDDVLLVPLAEPGVWVAEAEDEP LLT

SEQID No:238

VTIAFLRLITTLVKGQLGSTQSQGLVPCVMFVLKEMLPSYHKWRYNSHGVREQIGCLILE LIHAILNLCHETDLHSSHTPSLQFLCICSLAYTEAGQTVINIMGIGVDTIDMVMAAQPRSD GAEGQGQGQLLIKTVKLAFSVTNNVIRLKPPSNVVSPLEQALSQHGAHGNNLIAVLAKYI YHKHDPALPRLAIQLLKRLATVAPMSVYACLGNDAAAIRDAFLTRLQSKIEDMRIKVMILE

FLTVAVETQPGLIELFLNLEVKDGSDGSKEFSLGMWSCLHAVLELIDSQQQDRYWCPPL LHRAAIAFLHALWQDRRDSAMLVLRTKPKFWENLTSPLFGTLSPPSETSEPSILETCALI MKIICLEIYYVVKGSLDQSLKDTLKKFSIEKRFAYWSGYVKSLAVHVAETEGSSCTSLLEY QMLVSAWRMLLIIATTHADIMHLTDSVVRRQLFLDVLDGTKALLLVPASVNCLRLGSMKC TLLLILLRQWKRELGSVDEILGPLTEILEGVLQADQQLMEKTKAKVFSAFITVLQMKEMKV SDIPQYSQLVLNVCETLQEEVIALFDQTRHSLALGSATEDKDSMETDDCSRSRHRDQR DGVCVLGLHLAKELCEVDEDGDSWLQVTRRLPILPTLLTTLEVSLRMKQNLHFTEATLHL LLTLARTQQGATAVAGAGITQSICLPLLSVYQLSTNGTAQTPSASRKSLDAPSWPGVYR LSMSLMEQLLKTLRYNFLPEALDFVGVHQERTLQCLNAVRTVQSLACLEEADHTVGFIL QLSNFMKEWHFHLPQLMRDIQVGAQDGVLESGVMLGDREAVRSHWGTPSELQDVPE RGLFPWGAQGLLSCAYSG

SEQID No:239

MWERLNCAAEDFYSRLLQKFNEEKKGIRKDPFLYEADVQVQLISKGQPNPLKNILNENDI VFIVEKVPLEKEETSHIEELQSEETAISDFSTGENVGPLALPVGKARQLIGLYTMAHNPN MTHLKINLPVTALPPLWVRCDSSDPEGTCWLGAELITTNNSITGIVLYVVSCKADKNYSV NLENLKNLHKKRHHLSTVTSKGFAQYELFKSSALDDTITASQTAIALDISWSPVDEILQIP PLSSTATLNIKVESGEPRGPLNHLYRELKFLLVLADGLRTGVTEWLEPLEAKSAVELVQE FLNDLNKLDGFGDSTKKDTEVETLKHDTAAVDRSVKRLFKVRSDLDFAEQLWCKMSSS VISYQDLVKCFTLIIQSLQRGDIQPWLHSGSNSLLSKLIHQSYHGTMDTVSLSGTIPVQML LEIGLDKLKKDYISFFIGQELASLNHLEYFIAPSVDIQEQVYRVQKLHHILEILVSCMPFIKS QHELLFSLTQICIKYYKQNPLDEQHIFQLPVRPTAVKNLYQSEKPQKWRVEIYRGQKKIK TVWQLSDSSPIDHLNFHKPDFSELTLNGSLEERIFFTNMVTCSQVHFK

SEQID No:240

MPGMVLFGRRWAIASDDLVFPGFFELVVRVLWWIGILTLYLMHRGKLDCAGGALLSSYL IVLMILLAVVICTVSAIMCVSMRGTICNPGPRKSMSKLLYIRLALFFPEMVWASLGAAWVA DGVQCDRTVVNGIIATVVVSWIIIAATVVSIIIVFDPLGGKMAPYSSAGPSHLDSHDSSQLL NGLKTAATSVWETRIKLLCCCIGKDDHTRVAFSSTAELFSTYFSDTDLVPSDIAAGLALLH QQQDNIRNNQEPAQVVCHAPGSSQEADLDAELENCHHYMQFAAAAYGWPLYIYRNPL TGLCRIGGDCCRSRTTDYDLVGGDQLNCHFGSILHTTGLQYRDFIHVSFHDKVYELPFL VALDHRKESVVVAVRGTMSLQDVLTDLSAESEVLDVECEVQDRLAHKGISQAARYVYQ RLINDGILSQAFSIAPEYRLVIVGHSLGGGAAALLATMLRAAYPQVRCYAFSPPRGLWSK ALQEYSQSFIVSLVLGKDVIPRLSVTNLEDLKRRILRVVAHCNKPKYKILLHGLWYELFGG

NPNNLPTELDGGDQEVLTQPLLGEQSLLTRWSPAYSFSSDSPLDSSPKYPPLYPPGRII HLQEEGASGRFGCCSAAHYSAKWSHEAEFSKILIGPKMLTDHMPDILMRALDSVVSDR AACVSCPAQGVSSVDVA

SEQID No:241

MSSKEVKTALKSARDAIRNKEYKEALKHCKTVLKQEKNNYNAWVFIGVAAAELEQPDQA QSAYKKAAELEPDQLLAWQGLANLYEKYNHINAKDDLPGVYQKLLDLYESVDKQKWCD VCKKLVDLYYQEKKHLEVARTWHKLIKTRQEQGAENEELHQLWRKLTQFLAESTEDQN NETQQLLFTAFENALGLSDKIPSEDHQVLYRHFIQSLSKFPHESARLKKACEGMINIYPTV QYPLEVLCLHLIESGNLTDEGQQYCCRLVEMDSKSGPGLIGLGIKALQDKKYEDAVRNL TEGLKESPVCTSGWYHLAEAQVKMHRPKEAVLSCSQALKIVDNLGASGNSLYQRNLCL HLKAEALIKLSDYDSSEEAIRTLDQISDADNIPGLLVLKSLAYRNKGSFDEAAKIMEDLLSS YPDLAEVHALEALIHFTKKDYLQAEKCFQRALEKDTEVAEYHYQLGLTYWFMGEETRKD KTKALTHFLKAARLDTYMGKVFCYLGHYYRDVVGDKNRARGCYRKAFELDDTDAESGA AAVDLSVELEDMEMALAILTTVTQKASAGTAKWAWLRRGLYYLKAGQHSQAVADLQAA LRADPKDFNCWESLGEAYLSRGGYTTALKSFTKASELNPESIYSVFKVAAIQQILGKYKE AVAQYQMIIKKKEDYVPALKGLGECHLMMAKAALVDYLDGKAVDYIEKALEYFTCALQH RADVSCLWKLAGDACTCLYAVAPSKVNVHVLGVLLGQKEGKQVLKKNELLHLGGRCY GRALKLMSTSNTWCDLGINYYRQAQHLAETGSNMNDLKELLEKSLHCLKKAVRLDSNN HLYWNALGVVACYSGIGNYALAQHCFIKSIQSEQINAVAWTNLGVLYLTNENIEQAHEAF KMAQSLDPSYLMCWIGQALIAEAVGSYDTMDLFRHTTELNMHTEGALGYAYWVCTTLQ DKSNRETELYQYNILQMNAIPAAQVILNKYVERIQNYAPAFTMLGYLNEHLQLKKEAANA YQRAILLLQTAEDQDTYNVAIRNYGRLLCSTGEYDKAIQAFKSTPLEVLEDIIGFALALFM KGLYKESSKAYERALSIVESEQDKAHILTALAITEYKQGKTDVAKTLLFKCSILKEPTTESL QALCALGLAMQDATLSKAALNELLKHIKHKDSNYQRCLLTSAIYALQGRSVAVQKQISKA VHSNPGDPALWSLLSRVVAQYAQRNAKGGVVAGNVAHILDSNHGKKALLYTAVNQLA MGSSSAEDEKNTALKTIQKAALLSPGDPAIWAGLMAACHADDKLALVNNTQPKRIDLYL ALLSAVSASIKDEKFFENYNQSLEKWSLSQAVTGLIDTGRISEAETLCTKNLKSNPDQPA VILLERQVQCKPLLESQKPLPDAVLEELQKTVMSNSTSVPAWQWLAHVYQSQGMMRA AEMCYRKSLQLASQRGSWSGKLSSLLRLALLALKVCMANISNDHWPSLVQEATTEALK LCFCPLAVLLQALLQFKRKMGARETRRLLERVVYQPGYPKSIASTARWYLLRHLYAKDD YELIDVLVNNAKTHGDTRALELNQRLSSQ

MGAAAGRSPHLGPAPARRPQRSLLLLQLLLLVAAPGSTQAQAAPFPELCSYTWEAVDT KNNVLYKINICGSVDIVQCGPSSAVCMHDLKTRTYHSVGDSVLRSATRSLLEFNTTVSC DQQGTNHRVQSSIAFLCGKTLGTPEFVTATECVHYFEWRTTAACKKDIFKANKEVPCYV FDEELRKHDLNPLIKLSGAYLVDDSDPDTSLFINVCRDIDTLRDPGSQLRACPPGTAACL VRGHQAFDVGQPRDGLKLVRKDRLVLSYVREEAGKLDFCDGHSPAVTITFVCPSERRE GTIPKLTAKSNCRYEIEWITEYACHRDYLESKTCSLSGEQQDVSIDLTPLAQSGGSSYIS DGKEYLFYLNVCGETEIQFCNKKQAAVCQVKKSDTSQVKAAGRYHNQTLRYSDGDLTLI YFGGDECSSGFQRMSVINFECNKTAGNDGKGTPVFTGEVDCTYFFTWDTEYACVKEK **EDLLCGATDGKKRYDLSALVRHAEPEQNWEAVDGSQTETEKKHFFINICHRVLQEGKA** RGCPEDAAVCAVDKNGSKNLGKFISSPMKEKGNIQLSYSDGDDCGHGKKIKTNITLVCK PGDLESAPVLRTSGEGGCFYEFEWRTAAACVLSKTEGENCTVFDSQAGFSFDLSPLTK KNGAYKVETKKYDFYINVCGPVSVSPCQPDSGACQVAKSDEKTWNLGLSNAKLSYYD GMIQLNYRGGTPYNNERHTPRATLITFLCDRDAGVGFPEYQEEDNSTYNFRWYTSYAC PEEPLECVVTDPSTLEQYDLSSLAKSEGGLGGNWYAMDNSGEHVTWRKYYINVCRPL NPVPGCNRYASACQMKYEKDQGSFTEVVSISNLGMAKTGPVVEDSGSLLLEYVNGSA CTTSDGRQTTYTTRIHLVCSRGRLNSHPIFSLNWECVVSFLWNTEAACPIQTTTDTDQA CSIRDPNSGFVFNLNPLNSSQGYNVSGIGKIFMFNVCGTMPVCGTILGKPASGCEAETQ TEELKNWKPARPVGIEKSLQLSTEGFITLTYKGPLSAKGTADAFIVRFVCNDDVYSGPLK FLHQDIDSGQGIRNTYFEFETALACVPSPVDCQVTDLAGNEYDLTGLSTVRKPWTAVDT SVDGRKRTFYLSVCNPLPYIPGCQGSAVGSCLVSEGNSWNLGVVQMSPQAAANGSLSI MYVNGDKCGNQRFSTRITFECAQISGSPAFQLQDGCEYVFIWRTVEACPVVRVEGDNC EVKDPRHGNLYDLKPLGLNDTIVSAGEYTYYFRVCGKLSSDVCPTSDKSKVVSSCQEK REPQGFHKVAGLLTQKLTYENGLLKMNFTGGDTCHKVYQRSTAIFFYCDRGTQRPVFL KETSDCSYLFEWRTQYACPPFDLTECSFKDGAGNSFDLSSLSRYSDNWEAITGTGDPE HYLINVCKSLAPQAGTEPCPPEAAACLLGGSKPVNLGRVRDGPQWRDGIIVLKYVDGDL CPDGIRKKSTTIRFTCSESQVNSRPMFISAVEDCEYTFAWPTATACPMKSNEHDDCQVT NPSTGHLFDLSSLSGRAGFTAAYSEKGLVYMSICGENENCPPGVGACFGQTRISVGKA NKRLRYVDQVLQLVYKDGSPCPSKSGLSYKSVISFVCRPEAGPTNRPMLISLDKQTCTL FFSWHTPLACEQATECSVRNGSSIVDLSPLIHRTGGYEAYDESEDDASDTNPDFYINIC QPLNPMHAVPCPAGAAVCKVPIDGPPIDIGRVAGPPILNPIANEIYLNFESSTPCLADKHF NYTSLIAFHCKRGVSMGTPKLLRTSECDFVFEWETPVVCPDEVRMDGCTLTDEQLLYS FNLSSLSTSTFKVTRDSRTYSVGVCTFAVGPEQGGCKDGGVCLLSGTKGASFGRLQS MKLDYRHQDEAVVLSYVNGDRCPPETDDGVPCVFPFIFNGKSYEECIIESRAKLWCSTT

ADYDRDHEWGFCRHSNSYRTSSIIFKCDEDEDIGRPQVFSEVRGCDVTFEWKTKVVCP PKKLECKFVQKHKTYDLRLLSSLTGSWSLVHNGVSYYINLCQKIYKGPLGCSERASICR RTTTGDVQVLGLVHTQKLGVIGDKVVVTYSKGYPCGGNKTASSVIELTCTKTVGRPAFK RFDIDSCTYYFSWDSRAACAVKPQEVQMVNGTITNPINGKSFSLGDIYFKLFRASGDMR TNGDNYLYEIQLSSITSSRNPACSGANICQVKPNDQHFSRKVGTSDKTKYYLQDGDLDV VFASSSKCGKDKTKSVSSTIFFHCDPLVEDGIPEFSHETADCQYLFSWYTSAVCPLGVG FDSENPGDDGQMHKGLSERSQAVGAVLSLLLVALTCCLLALLLYKKERRETVISKLTTC CRRSSNVSYKYSKVNKEEETDENETEWLMEEIQLPPPRQGKEGQENGHITTKSVKALS SLHGDDQDSEDEVLTIPEVKVHSGRGAGAESSHPVRNAQSNALQEREDDRVGLVRGE KARKGKSSSAQQKTVSSTKLVSFHDDSDEDLLHI

SEQID No:243

MSDKMSSFLHIGDICSLYAEGSTNGFISTLGLVDDRCVVQPETGDLNNPPKKFRDCLFK LCPMNRYSAQKQFWKAAKPGANSTTDAVLLNKLHHAADLEKKQNETENRKLLGTVIQY GNVIQLLHLKSNKYLTVNKRLPALLEKNAMRVTLDEAGNEGSWFYIQPFYKLRSIGDSVV IGDKVVLNPVNAGQPLHASSHQLVDNPGCNEVNSVNCNTSWKIVLFMKWSDNKDDILK **GGDVVRLFHAEQEKFLTCDEHRKKQHVFLRTTGRQSATSATSSKALWEVEVVQHDPC** RGGAGYWNSLFRFKHLATGHYLAAEVDPDFEEECLEFQPSVDPDQDASRSRLRNAQE KMVYSLVSVPEGNDISSIFELDPTTLRGGDSLVPRNSYVRLRHLCTNTWVHSTNIPIDKE EEKPVMLKIGTSPVKEDKEAFAIVPVSPAEVRDLDFANDASKVLGSIAGKLEKGTITQNE RRSVTKLLEDLVYFVTGGTNSGQDVLEVVFSKPNRERQKLMREQNILKQIFKLLQAPFT DCGDGPMLRLEELGDQRHAPFRHICRLCYRVLRHSQQDYRKNQEYIAKQFGFMQKQI GYDVLAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRKNREPRFLDYLSDLCVSMNKSIP VTQELICKAVLNPTNADILIETKLVLSRFEFEGVSSTGENALEAGEDEEEVWLFWRDSNK EIRSKSVRELAQDAKEGQKEDRDVLSYYRYQLNLFARMCLDRQYLAINEISGQLDVDLIL RCMSDENLPYDLRASFCRLMLHMHVDRDPQEQVTPVKYARLWSEIPSEIAIDDYDSSG ASKDEIKERFAQTMEFVEEYLRDVVCQRFPFSDKEKNKLTFEVVNLARNLIYFGFYNFS DLLRLTKILLAILDCVHVTTIFPISKMAKGEENKGNNDVEKLKSSNVMRSIHGVGELMTQV VLRGGGFLPMTPMAAAPEGNVKQAEPEKEDIMVMDTKLKIIEILQFILNVRLDYRISCLLCI **FKREFDESNSQTSETSSGNSSQEGPSNVPGALDFEHIEEQAEGIFGGSEENTPLDLDD HGGRTFLRVLLHLTMHDYPPLVSGALQLLFRHFSQRQEVLQAFKQVQLLVTSQDVDNY** KQIKQDLDQLRSIVEKSELWVYKGQGPDETMDGASGENEHKKTEEGNNKPQKHESTS SYNYRVVKEILIRLSKLCVQESASVRKSRKQQQRLLRNMGAHAVVLELLQIPYEKAEDTK MOEIMBLAHEFLONFCAGNOQNQALLHKHINLFLNPGILEAVTMQHIFMNNFQLCSEINE

RVVQHFVHCIETHGRNVQYIKFLQTIVKAEGKFIKKCQDMVMAELVNSGEDVLVFYNDR **ASFQTLIQMMRSERDRMDENSPLMYHIHLVELLAVCTEGKNVYTEIKCNSLLPLDDIVRV** VTHEDCIPEVKIAYINFLNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNNTSDRK HADSILEKYVTEIVMSIVTTFFSSPFSDQSTTLQTRQPVFVQLLQGVFRVYHCNWLMPS QKASVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKSHSIVQKTAMNWRLSARNAARR DSVLAASRDYRNIIERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELLFPENTDARRKC ESGGFICKLIKHTKQLLEENEEKLCIKVLQTLREMMTKDRGYGEKLISIDELDNAELPPAP DSENSTEELEPSPPLRQLEDHKRGEALRQVLVNRYYGNVRPSGRRESLTSFGNGPLSA GGPGKPGGGGGGSGSSSMSRGEMSLAEVQCHLDKEGASNLVIDLIMNASSDRVFHES ILLAIALLEGGNTTIQHSFFCRLTEDKKSEKFFKVFYDRMKVAQQEIKATVTVNTSDLGNK KKDDEVDRDAPSRKKAKEPTTQITEEVRDQLLEASAATRKAFTTFRREADPDDHYQPG EGTQATADKAKDDLEMSAVITIMQPILRFLQLLCENHNRDLQNFLRCQNNKTNYNLVCE TLQFLDCICGSTTGGLGLLGLYINEKNVALINQTLESLTEYCQGPCHENQNCIATHESNGI DIITALILNDINPLGKKRMDLVLELKNNASKLLLAIMESRHDSENAERILYNMRPKELVEVI KKAYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQLARHNKELQSMLKPGGQVDG DEALEFYAKHTAQIEIVRLDRTMEQIVFPVPSICEFLTKESKLRIYYTTERDEQGSKINDFF LRSEDLFNEMNWQKKLRAQPVLYWCARNMSFWSSISFNLAVLMNLLVAFFYPFKGVR **GGTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALIASTILRLIFSVGLQPTLFLLGAFNVCN** KIIFLMSFVGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLFVHEFFYSLLLFDLVYREE TLLNVIKSVTRNGRSIILTAVLALILVYLFSIVGYLFFKDDFILEVDRLPNETAVPETGESLA SEFLFSDVCRVESGENCSSPAPREELVPAEETEQDKEHTCETLLMCIVTVLSHGLRSGG GVGDVLRKPSKEEPLFAARVIYDLLFFFMVIIIVLNLIFGVIIDTFADLRSEKQKKEEILKTTC FICGLERDKFDNKTVTFEEHIKEEHNMWHYLCFIVLVKVKDSTEYTGPESYVAEMIKERN LDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRK QKQRIGLLGHPPHMNVNPQQPA

SEQID No:244

GGRQRCQRGRSCGAREEEVEPGTARPPPAASAMDASLEKIADPTLAEMGKNLKEAVK MLEDSQRRTEEENGKKLISGDIPGPLQGSGQDMVSILQLVQNLMHGDEDEEPQSPRIQ NIGEQGHMALLGHSLGAYISTLDKEKLRKLTTRILSDTTLWLCRIFRYENGCAYFHEEER EGLAKICRLAIHSRYEDFVVDGFNVLYNKKPVIYLSAAARPGLGQYLCNQLGLPFPCLCR VPCNTVFGSQHQMDVAFLEKLIKDDIERGRLPLLLVANAGTAAVGHTDKIGRLKELCEQ YGIWLHVEGVNLATLALGYVSSSVLAAAKCDSMTMTPGPWLGLPAVPAVTLYKHDDPA LTLVAGLTSNKPTDKLRALPLWLSLQYLGLDGFVERIKHACQLSQRLQESLKKVNYIKILV

EDELSSPVVVFRFFQELPGSDPVFKAVPVPNMTPSGVGRERHSCDALNRWLGEQLKQ LVPASGLTVMDLEAEGTCLRFSPLMTAAVLGTRGEDVDQLVACIESKLPVLCCTLQLRE -EFKQEVEATAGLLYVDDPNWSGIGVVRYEHANDDKSSLKSDPEGENIHAGLLKKLNELE SDLTFKIGPEYKSMKSCLYVGMASDNVDAAELVETIAATAREIEENSRLLENMTEVVRKG IQEAQVELQKASEERLLEEGVLRQIPVVGSVLNWFSPVQALQKGRTFNLTAGSLESTEPI YVYKAQGAGVTLPPTPSGSRTKQRLPGQKPFKRSLRGSDALSETSSVSHIEDLEKVERL SSGPEQITLEASSTEGHPGAPSPQHTDQTEAFQKGVPHPEDDHSQVEGPESLR

SEQID No:245

EPCALTPGPSHLALTFLPSKPGARPQPEGASWDAGPGGAPSAWADPGEGGPSPMLLP EGLSSQALSTEAPLPATLEPRIVMGEETCQALLSPRAARTALRDQEGGHASPDPPPELC SQGDLSVPSPPPDPDSFFTPPSTPTKTTYALLPACGPHGDARDSEAELRDELLDSPPAS PSGSYITADGDSWASSPSCSLSLLAPAEGLDFPSGWGLSPQGSMVDERELHPAGTPE PPSSESSLSADSSSSWGQEGHFFDLDFLANDPMIPAALLPFQGSLIFQVEAVEVTPLSP EEEEEAVADPDPGGDLAGEGEEDSTSASFLQSLSDLSITEGMDEAFAFRDDTSAASS DSDSASYAEADDERLYSGEPHAQATLLQDSVQKTEEESGGGAKGLQAQDGTVSWAVE **AAPQTSDRGAYLSQRQELISEVTEEGLALGQESTATVTPHTLQVAPGLQVEVATRVTPQ** AGEEETDSTAGQESAAMAMPQPSQEGISEILGQESVTAEKLPTPQEETSLTLCPDSPQ NLKEEGGLDLPSGRKPVAAATIVPRQAKEDLTLPQDSAMTPPLPLQDTDLSSAPKPVAA ATIVSQQAEEGLTLPQDSVMTPPLPLQDTELSSAPKPVAAATLVSQQAEEGLTLPQDSA MTPPLPLQDTDLSSAPKPVAAATLVSQQAEEGLTLPQDSAMTPPLPLQDTDLSSAPKPV AAATLVSQQAEEGLTLPQDSAMTPPLPLQDTDLSSAPKPVAAATIVSQQAEEGLTLPQD SAMTPPLPLQDTDLSSAPKPVAAATIVSQQAEEGLTLPQDSAMTPPLPLQDTDLSSAPK PVAAATPVSQQAEEGLTLPQDSAMTPPLPLQDTDLSSAPKPVAAATPVSQQAEEGLTL PQDSAMTAPLPLQDTGPTSGPEPLAVATPQTLQAEAGCAPGTEPVATMAQQEVGEAL GPRPAPEEKNAALPTVPEPAALDQVQQDDPQPAAEAGTPWAAQEDADSTLGMEALSL PEPASGAGEEIAEALSRPGREACLEARAHTGDGAKPDSPQKETLEVENQQEGGLKLLA QEHGPRSALGGAREVPDAPPAACPEVSQARLLSPAREERGLSGKSTPEPTLPSAVATE ASLDSCPESSVGAVSSLDRGCPDAPAPTSAPTSQQPEPVLGLGSVEQPHEVPSVLGTP LLQPPENLAKGQPSTPVDRPLGPDPSAPGTLAGAALPPLEPPAPCLCQDPQEDSVEDE EPPGSLGLPPPQAGVQPAAAAVSGTTQPLGTGPRVSLSPHSPLLSPKVASMDAKDLAL QILPPCQVPPPSGPQSPAGPQGLSAPEQQEDEDSLEEDSPRALGSGQHSDSHGESSA ELDEQDILAPQTVQCPAQAPAGGSEETIAKAKQSRSEKKARKAMSKLGLRQIQGVTRITI QKSKNILFVIAKPDVFKSPASDTYVVFGEAKIEDLSQQVHKAAAEKFKVPSEPSALVPES

APRPRVRLECKEEEEEEEVDEAGLELRDIELVMAQANVSRAKAVRALRDNHSDIVNA IMELTM

SEQID No:246

MLTTLKPFGSVSVESKMNNKAGSFFWNLRQFSTLVSTSRTMRLCCLGLCKPKIVHSNW NILNNFHNRMQSTDIIRYLFQDAFIFKSDVGFQTKGISTLTALRIERLLYAKRLFFDSKQSL VPVDKSDDELKKVNLNHEVSNEDVLTKETKPNRISSRKLSEECNSLSDVLDAFSKAPTF PSSNYFTAMWTIAKRLSDDQKRFEKRLMFSHPAFNQLCEHMMREAKIMQYKYLLFSLH AIVKLGIPQNTILVQTLLRVTQERINECDEICLSVLSTVLEAMEPCKNVHVLRTGFRILVDQ QVWKIEDVFTLQVVMKCIGKDAPIALKRKLEMKALRELDRFSVLNSQHMFEVLAAMNHR SLILLDECSKVVLDNIHGCPLRIMINILQSCKDLQYHNLDLFKGLADYVAATFDIWKFRKVL FILILFENLGFRPVGLMDLFMKRIVEDPESLNMKNILSILHTYSSLNHVYKCQNKEQFVEV MASALTGYLHTISSENLLDAVYSFCLMNYFPLAPFNQLLQKDIISELLTSDDMKNAYKLHT LDTCLKLDDTVYLRDIALSLPQLPRELPSSHTNAKVAEVLSSLLGGEGHFSKDVHLPHNY HIDFEIRMDTNRNQVLPLSDVDTTSATDIQRLLTYISFAGLSELKS

SEQID No:247

LQLSVKMSVLISQSVINYVEEENIPALKALLEKCKDVDERNECGQTPLMIAAEQGNLEIVK ELIKNGANCNLEDLDNWTALISASKEGHVHIVEELLKCGVNLEHRDMGGWTALMWACY KGRTDVVELLLSHGANPSVTGLYSVYPIIWAAGRGHADIVHLLLQNGAKVNCSDKYGTT PLVWAARKGHLECVKHLLAMGADVDQEGANSMTALIVAVKGGYTQSVKEILKRNPNVN LTDKDGNTALMIASKEGHTEIVQDLLDAGTYVNIPDRSGDTVLIGAVRGGHVEIVRALLQ KYADIDIRGQDNKTALYWAVEKGNATMVRDILQCNPDTEICTKDGETPLIKATKMRNIEV **VELLLDKGAKVSAVDKKGDTPLHIAIRGRSRKLAELLLRNPKDGRLLYRPNKAGETPYNI** DCSHQKSILTQIFGARHLSPTETDGDMLGYDLYSSALADILSEPTMQPPICVGLYAQWG SGKSFLLKKLEDEMKTFAGQQIEPLFQFSWLIVFLTLLLCGGLGLLFAFTVHPNLGIAVSL SFLALLYIFFIVIYFGGRREGESWNWAWVLSTRLARHIGYLELLLKLMFVNPPELPEQTTK ALPVRFLFTDYNRLSSVGGETSLAEMIATLSDACEREFGFLATRLFRVFKTEDTQGKKK WKKTCCLPSFVIFLFIIGCIISGITLLAIFRVDPKHLTVNAVLISIASVVGLAFVLNCRTWWQ VLDSLLNSQRKRLHNAASKLHKLKSEGFMKVLKCEVELMARMAKTIDSFTQNQTRLVVII DGLDACEQDKVLQMLDTVRVLFSKGPFIAIFASDPHIIIKAINQNLNSVLRDSNINGHDYM RNIVHLPVFLNSRGLSNARKFLVTSATNGDVPCSDTTGIQEDADRRVSQNSLGEMTKLG SKTALNRRDTYRRRQMQRTITRQMSFDLTKLLVTEDWFSDISPQTMRRLLNIVSVTGRL LRANQISFNWDRLASWINLTEQWPYRTSWLILYLEETEGIPDQMTLKTIYERISKNIPTTK

DVEPLLEIDGDIRNFEVFLSSRTPVLVARDVKVFLPCTVNLDPKLREIIADVRAAREQISIG GLAYPPLPLHEGPPRAPSGYSQPPSVCSSTSFNGPFAGGVVSPQPHSSYYSGMTGPQ HPFYNRPFFAPYLYTPRYYPGGSQHLISRPSVKTSLPRDQNNGLEVIKEDAAEGLSSPT DSSRGSGPAPGPVVLLNSLNVDAVCEKLKQIEGLDQSMLPQYCTTIKKANINGRVLAQC NIDELKKEMNMNFGDWHLFRSTVLEMRNAESHVVPEDPRFLSESSSGPAPHGEPARR ASHNELPHTELSSQTPYTLNFSFEELNTLGLDEGAPRHSNLSWQSQTRRTPSLSSLNS QDSSIEISKLTDKVQAEYRDAYREYIAQMSQLEGGPGSTTISGRSSPHSTYYMGQSSSG GSIHSNLEQEKGKDSEPKPDDGRKSFLMKRGDVIDYSSSGVSTNDASPLDPITEEDEKS DQSGSKLLPGKKSSERSSLFQTDLKLKGSGLRYQKLPSDEDESGTEESDNTPLLKDDK DRKAEGKVERVPKSPEHSAEPIRTFIKAKEYLSDALLDKKDSSDSGVRSSESSPNHSLH NEVADDSQLEKANLIELEDDSHSGKRGIPHSLSGLQDPIIARMSICSEDKKSPSECSLIAS SPEENWPACQKAYNLNRTPSTVTLNNNSAPANRANQNFDEMEGIRETSQVILRPSSSP NPTTIQNENLKSMTHKRSQRSSYTRLSKDPPELHAAASSESTGFGEERESIL

SEQID No:248

MEAAPPGPPWPLLLLLLLLALCGCPAPAAASPLLLFANRRDVRLVDAGGVKLESTIVVS GLEDAAAVDFQFSKGAVYWTDVSEEAIKQTYLNQTGAAVQNVVISGLVSPDGLACDWV GKKLYWTDSETNRIEVANLNGTSRKVLFWQDLDQPRAIALDPAHGYMYWTDWGETPRI **ERAGMDGSTRKIIVDSDIYWPNGLTIDLEEQKLYWADAKLSFIHRANLDGSFRQKVVEG** SLTHPFALTLSGDTLYWTDWQTRSIHACNKRTGGKRKEILSALYSPMDIQVLSQERQPF FHTRCEEDNGGCSHLCLLSPSEPFYTCACPTGVQLQDNGRTCKAGAEEVLLLARRTDL RRISLDTPDFTDIVLQVDDIRHAIAIDYDPLEGYVYWTDDEVRAIRRAYLDGSGAQTLVNT EINDPDGIAVDWVARNLYWTDTGTDRIEVTRLNGTSRKILVSEDLDEPRAIALHPVMGLM YWTDWGENPKIECANLDGQERRVLVNASLGWPNGLALDLQEGKLYWGDAKTDKIEVIN VDGTKRRTLLEDKLPHIFGFTLLGDFIYWTDWQRRSIERVHKVKASRDVIIDQLPDLMGL KAVNVAKVVGTNPCADRNGGCSHLCFFTPHATRCGCPIGLELLSDMKTCIVPEAFLVFT SRAAIHRISLETNNNDVAIPLTGVKEASALDFDVSNNHIYWTDVSLKTISRAFMNGSSVE HVVEFGLDYPEGMAVDWMGKNLYWADTGTNRIEVARLDGQFRQVLVWRDLDNPRSL ALDPTKGYIYWTEWGGKPRIVRAFMDGTNCMTLVDKVGRANDLTIDYADQRLYWTDLD TNMIESSNMLGQERVVIADDLPHPFGLTQYSDYIYWTDWNLHSIERADKTSGRNRTLIQ GHLDFVMDILVFHSSRQDGLNDCMHNNGQCGQLCLAIPGGHRCGCASHYTLDPSSRN CSPPTTFLLFSQKSAISRMIPDDQHSPDLILPLHGLRNVKAIDYDPLDKFIYWVDGRQNIK RAKDDGTQPFVLTSLSQGQNPDRQPHDLSIDIYSRTLFWTCEATNTINVHRLSGEAMGV VLRGDRDKPRAIVVNAERGYLYFTNMQDRAAKIERAALDGTEREVLFTTGLIRPVALVVD NTLGKLFWVDADLKRIESCDLSGANRLTLEDANIVQPLGLTILGKHLYWIDRQQMIERV EKTTGDKRTRIQGRVAHLTGIHAVEEVSLEEFSAHPCARDNGGCSHICIAKGDGTPRCS CPVHLVLLQNLLTCGEPPTCSPDQFACATGEIDCIPGAWRCDGFPECDDQSDEEGCPV CSAAQFPCARGQCVDLRLRCDGEADCQDRSDEVDCDAICLPNQFRCASGQCVLIKQQ CDSFPDCIDGSDELMCEITKPPSDDSPAHSSAIGPVIGIILSLFVMGGVYFVCQRVVCQR YAGANGPFPHEYVSGTPHVPLNFIAPGGSQHGPFTGIACGKSMMSSVSLMGGRGGVP LYDRNHVTGASSSSSSSTKATLYPPILNPPPSPATDPSLYNMDMFYSSNIPATARPYRP YIIRGMAPPTTPCSTDVCDSDYSASRWKASKYYLDLNSDSDPYPPPPTPHSQYLSAEDS CPPSPATERSYFHLFPPPPSPCTDSS

SEQID No:249

MDMFPLTWVFLALYFSRHQVRGQPDPPCGGRLNSKDAGYITSPGYPQDYPSHQNCE WIVYAPEPNQKIVLNFNPHFEIEKHDCKYDFIEIRDGDSESADLLGKHCGNIAPPTIISSGS MLYIKFTSDYARQGAGFSLRYEIFKTGSEDCSKNFTSPNGTIESPGFPEKYPHNLDCTFT ILAKPKMEIILQFLIFDLEHDPLQVGEGDCKYDWLDIWDGIPHVGPLIGKYCGTKTPSELR SSTGILSLTFHTDMAVAKDGFSARYYLVHQEPLENFQCNVPLGMESGRIANEQISASST YSDGRWTPQQSRLHGDDNGWTPNLDSNKEYLQVDLRFLTMLTAIATQGAISRETQNG YYVKSYKLEVSTNGEDWMVYRHGKNHKVFQANNDATEVVLNKLHAPLLTRFVRIRPQT WHSGIALRLELFGCRVTDAPCSNMLGMLSGLIADSQISASSTQEYLWSPSAARLVSSRS **GWFPRIPQAQPGEEWLQVDLGTPKTVKGVIIQGARGGDSITAVEARAFVRKFKVSYSLN** GKDWEYIQDPRTQQPKLFEGNMHYDTPDIRRFDPIPAQYVRVYPERWSPAGIGMRLEV LGCDWTDSKPTVETLGPTVKSEETTTPYPTEEEATECGENCSFEDDKDLQLPSGFNCN FDFLEEPCGWMYDHAKWLRTTWASSSSPNDRTFPDDRNFLRLQSDSQREGQYARLIS PPVHLPRSPVCMEFQYQATGGRGVALQVVREASQESKLLWVIREDQGGEWKHGRIILP SYDMEYQIVFEGVIGKGRSGEIAIDDIRISTDVPLENCMEPISAFAGENFKVDIPEIHEREG YEDEIDDEYEVDWSNSSSATSGSGAPSTDKEKSWLYTLDPILITIIAMSSLGVLLGATCA GLLLYCTCSYSGLSSRSCTTLENYNFELYDGLKHKVKMNHQKCCSEA

SEQID No:250

MVSRCSCLGVQCLLLSLLLLAAWEVGSGQLHYSVYEEARHGTFVGRIAQDLGLELAELV QRLFRVASKRHGDLLEVNLQNGILFVNSRIDREELCGRSVECSIHLEVIVDRPLQVFHVD VEVKDINDNPPRFSVTEQKLSIPESRLLDSRFPLEGASDADVGENALLTYKLSPNEYFVL DIINKKDKDKFPVLVLRKLLDREENPQLKLLLTATDGGKPEFTGSVSLLILVLDANDNAPIF DRPVYEVKMYENQVNQTLVIRLNASDSDEGINKEMMYSFSSLVPPTIRRKFWINERTGEI

SEQID No:251

MENGGAGTLQIRQVLLFFVLLGMSQAGSETGNFLVMEELQSGSFVGNLAKTLGLEVSE LSSRGARVVSNDNKECLQLDTNTGDLLLREMLDREELCGSNEPCVLYFQVLMKNPTQF LQIELQVRDINDHSPVFLEKEMLLEIPENSPVGAVFLLESAKDLDVGINAVKSYTINPNSH FHVKIRVNPDNRKYPELVLDKALDYEERPELSFILTALDGGSPPRSGTALVRVVVVDIND NSPEFEQAFYEVKILENSILGSLVVTVSAWDLDSGTNSELSYTFSHASEDIRKTFEINQKS GDITLTAPLDFEAIESYSIIIQATDGGGLFGKSTVRIQVMDVNDNAPEITVSSITSPIPENTP ETVVMVFRIRDRDSGDNGKMVCSIPEDIPFVLKSSVNNYYTLETERPLDRESRAEYNITI TVTDLGTPRLKTEHNITVLVSDVNDNAPAFTQTSYALFVRENNSPALHIGSISATDRDSG TNAQVNYSLLPSQDPHLPLASLVSINADNGHLFALRSLDYEALQGFQFRVGATDHGSPA LSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPWAAEPGYLVTKVVAVDGDSGQ NAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATA TLHVLLVDGFSQPYLPLPEAAPAQAQADSLTVYLVVALASVSSLFLFSVLLFVAVRLCRR SRAAPVGRCSVPEGPFPGHLVDVSGTGTLSQSYHYEVCVTGGSRSNKFKFLKPIIPNFL PQSTGSEVEENPPFQNNLGF

SEQID No:252

MEASGKLICROROVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEORE FSRRGVRVVSRGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLRFQVLLESPFEFF QAELQVIDINDHSPVFLDKQMLVKVSESSPPGTTFPLKNAEDLDVGQNNIENYIISPNSYF RVLTRKRSDGRKYPELVLDKALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVLDVND NAPEFEQPFYRVQISEDSPVGFLVVKVSATDVDTGVNGEISYSLFQASEEIGKTFKINPL
TGEIELKKQLDFEKLQSYEVNIEARDAGTFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPE
NAPETVVALFSVSDLDSGENGKISCSIQEDLPFLLKSAENFYTLLTERPLDRESRAEYNIT
ITVTDLGTPMLITQLNMTVLIADVNDNAPAFTQTSYTLFVRENNSPALHIRSVSATDRDSG
TNAQVTYSLLPPQDPHLPLTSLVSINADNGHLFALRSLDYEALQGFQFRVGASDHGSPA
LSSEALVRVVVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQ
NAWLSYQLLKATELGLFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATA
TLHVLLVDGFSQPYLPLPEAAPTQAQADLLTVYLVVALASVSSLFLFSVLLFVAVRLCRR
SRAASVGRCLVPEGPLPGHLVDMSGTRTLSQSYQYEVCLAGGSGTNEFKFLKPIIPNFP
PQCPGKEIQGNSTFPNNFGFNIQ

SEQID No:253

MKKLGRIHPNRQVLAFILMVFLSQVRLEPIRYSVLEETESGSFVAHLAKDLGLGIGELASR SARVLSDDDKQRLQLDRQTGDLLLREKLDREELCGPIEPCVLHFQVFLEMPVQFFQGEL LIQDINDHSPIFPEREVLLKILENSQPGTLFPLLIAEDLDVGSNGLQKYTISPNSHFHILTRN HSEGKKYPDLVQDKPLDREEQPEFSLTLVALDGGSPPRSGTVMVRILIMDINDNAPEFV HTPYGVQVLENSPLDSPIVRVLARDIDAGNFGSVSYGLFQASDEIKQTFSINEVTGEILLK KKLDFEKIKSYHVEIEATDGGGLSGKGTVVIEVVDVNDNPPELIISSLTSSIPENAPETVVS IFRIRDRDSGENGKMICSIPDNLPFILKPTLKNFYTLVTERPLDRETSAEYNITIAVTDLGTP RLKTQQNITVQVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDRDSGTNAQVTY SLLPPQDPHLPLASLVSINADNGHLFALRSLDYEALQAFEFRVGASDRGSPALSSEALV RVLVLDTNDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQNAWLSYQ LLKATEPGLFGVWAHNGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATATLHVLLVD GFSQPYLPLPEAAPAQAQADSLTVYLVVALASVSSLFLFSVLLFVAVRLCRRSRAASVG RCSVPEGPFPGHLVDVSGTGTLSQSYQYEVCLTGDSGTGEFKFLKPIFPNLLVQDTGR EVKENPKFRNSLVFS

SEQID No:254

MQRAREAEMMKSQVLFPFLLSLFCGAISQQIRYTIPEELANGSRVGKLAKDLGLSVREL PTRKLRVSAEDYFNVSLESGDLLVNGRIDREKICGRKLECALEFETVAENPMNVFHVVV VIQDINDNAPRFVAKGIDLEICESALPGVKFSLDSAQDADVEGNSLKLYTINPNQYFSLST KESPDGSKYPVLLLEKPLDREHQSSHRLILTAMDGGDPPLSGTTHIWIRVTDANDNAPV FSQEVYRVSLQENVPWGTSVLRVMATDQDEGINAEITYAFLNSPISTSLFNLNPNTGDIT TNGTLDFEETSRYVLSVEAKDGGVHTAHCNVQIEIVDENDNAPEVTFMSFSNQIPEDSD

LGTVIALIKVRDKDSGQNGMVTCYTQEEVPFKLESTSKNYYKLVIAGALNREQTADYNVT
IIATDKGKPALSSRTSITLHISDINDNAPVFHQASYVVHVSENNPPGASIAQVSASDPDLG
PNGRVSYSILASDLEPRELLSYVSVSPQSGVVFAQRAFDHEQLRAFELTLQARDQGSPA
LSANVSLRVLVGDLNDNAPRVLYPALGPDGSALFDMVPRAAEPGYLVTKVVAVDADSG
HNAWLSYHVLQASEPGLFSLGLRTGEVRTARALGDRDAARQRLLVAVRDGGQPPLSA
TATLHLIFADSLQEVLPDLSDRPEPSDPQTELQFYLVVALALISVLFLLAVILAIALRLRRSS
SLDTEGCFQTGLCSKSGPGVPPNHSEGTLPYSYNLCIASHSAKTEFNSLNLTPEMAPPQ
DLLCDDPSMVVCASNEDHKIAYDPSLSSHQAPPNTDWRFSQAQRPGTSGSQNGDDTG
TWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQFTLQHVPDYRQ
NVYIPGSNATLTNAAGKRDGKAPAGGNGNKKKSGKKEKK

SEQID No:255

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MGGSCAQRRAGPRQVLFPLLLPLFYPTLSEPIRYSIPEELAKGSVVGNLAKDLGLSVLD VSARKLRVSAEKLHFSVDAESGDLLVKNRIDREQICKERRRCELQLEAVVENPLNIFHVI VVIEDVNDHAPQFDKKEIHLEIFESASAGTRLSLDPATDPDININSIKDYKINSNPYFSLMV RVNSDGGKYPELSLEKLLDREEQRSHSLILTALDGGDPPRSATAHIEISVKDTNDNPPVF SRDEYRISLSENLPPGSPVLQVTATDQDEGVNAEINYYFRSTAQSTKHMFSLDEKTGMI KNNQSFDFEDVERYTMEVEAKDGGGLSTQCKVIIEILDENDNSPEIIITSLSDQILENSPP GMVVALFKTRDLDFGGNGEVRCNIETDIPFKIYSSSNNYYKLVTDGALDREQTPEYNVTI VATDRGKPPLSSSRSITLYVADINDNAPVFDQTSYVVHVAENNPPGASIAQVSASDPDL GLNGHISYSIVASDLEPLAVSSYVSVSAQSGVVFAQRAFDHEQLRAFALTLQARDHGSP TLSANVSLRVLVGDRNDNAPRVLYPALGPDGSAFFDMVPRSAEPGYLVTKVVAVDADS GHNAWLSYHVLQASEPGLFSLGLRTGEVRTARALGDRDAARQRLLVAVRDGGQPPLS ATATLHLVFADNLQEILPDLSDRPVLSDPQAELQFYLVVALALISVLFLLAVILAIALRLRRS LSPATWDCFHPGLCVKSGPVVPPNYSEGTLPYSYNLCIAHTGTKEFNFLKCSVPLHSNE DMVCSVSPGALIPPHGGEDLTSHPETLTSQAPPNTDWRFSQAQRPGTSGSQNGDDTG TWPNNQFDTEMLQAMILASASEAADGSSTLGGGAGTMGLSARYGPQFTLQHVPDYRQ NVYIPGSNATLTNAAGKRDGKAPAGGNGNKKKSGKKEKK

SEQID No:256

MAAAAARVVLSSAARGGLWGFSESLLIRGAAGRSLYFGENRLRSTQAATQVVLNVPET RVTCLESGLRVASEDSGLSTCTVGLWIDAGSRYENEKNNGTAHFLEHMAFKGTKKRSQ LDLELEIENMGAHLNAYTSREQTVYYAKAFSKDLPRAVEILADIIQNSTLGEAEIERERGVI LREMQEVETNLQEVVFDYLHATAYQNTALGRTILGPTENIKSISRKDLVDYITTHYKGPRI VLAAAGGVSHDELLDLAKFHFGDSLCTHKGEIPALPPCKFTGSEIRVRDDKMPLAHLAIA VEAVGWAHPDTICLMVANTLIGNWDRSFGGGMNLSSKLAQLTCHGNLCHSFQSFNTSY TDTGLWGLYMVCESSTVADMLHVVQKEWMRLCTSVTESEVARARNLLKTNMLLQLDG STPICEDIGRQMLCYNRRIPIPELEARIDAVNAETIREVCTKYIYNRSPAIAAVGPIKQLPDF KQIRSNMCWLRD

SEQID No:257

MGAYLSQPNTVKCSGDGVGAPRLPLPYGFSAMQGWRVSMEDAHNCIPELDSETAMFS
VYDGHGGEEVALYCAKYLPDIIKDQKAYKEGKLQKALEDAFLAIDAKLTTEEVIKELAQIA
GRPTEDEDEKEKVADEDDVDNEEAALLHEEATMTIEELLTRYGQNCHKGPPHSKSGGG
TGEEPGSQGLNGEAGPEDSTRETPSQENGPTAKAYTGFSSNSERGTEAGQVGEPGIP
TGEAGPSCSSASDKLPRVAKSKFFEDSEDESDEAEEEEEDSEECSEEEDGYSSEEAEN
EEDEDDTEEAEEDDEEEEEEMMVPGMEGKEEPGSDSGTTAVVALIRGKQLIVANAGDS
RCVVSEAGKALDMSYDHKPEDEVELARIKNAGGKVTMDGRVNGGLNLSRAIGDHFYKR
NKNLPPEEQMISALPDIKVLTLTDDHEFMVIACDGIWNVMSSQEVVDFIQSKISQRDENG
ELRLLSSIVEELLDQCLAPDTSGDGTGCDNMTCIIICFKPRNTAELQPESGKRKLEEVLST
EGAEENGNSDKKKKAKRD

SEQID No:258

MMETPLPKAPEKRQVTAIIFLLLLWEAGSATIKYSVLEERDSGSFVANLAKDLGLGVGEL AARGARILSKGNKQYLQLERKSGNLLLKEKLDREELCGDIDPCILHFQMLLKNPVQFIQG ELQLQDVNDHAPEFLENEILLKISEGSHPGTSFPLKIAQDLDVGSNTVQNYSISTNSYFHL FTRNHSDGKKYPELVLDQALDREEQPQLRLTLTALDGGSPPRTGTSQVLIVIVDINDNVP EFAQRRYEVQVPENTPIGSLVITVSARDLDAGTHGELSYSFFQYSNQIIQAFEINSITGEIR FKKALDFEEIQSYHMEVEASDGGGLSGKCTVAIEVMDINDNAPELTMSLLISDILENSPET VVAVFGISDPDSGNNGKMMCSIQDHLPFLLKPTLENFYTLLTEGALDRESRAEYNITITVT DLGTPRLKTEYNITLRVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDRDSGTN AQVTYSLLPPQNPHLPLASLVSINTDNGHLFALRSLDYEALQEFEFRVGASDRGSPALS SEALVRVLVCWTPTTTRPSCCTRCRTAPRPAPSWCPGRPSRATW

SEQID No:259

MLRMRTAGWARGWCLGCCLLLPLSFSLAAAKQLLRYRLAEEGPADVRIGNVASDLGIV TGSGEVTFSLESGSEYLKIDNLTGELSTSERRIDREKLPQCQMIFDENECFLDFEVSVIG PSQSWVDLFEGQVIVLDINDNTPTFPSPVLTLTVEENRPVGTLYLLPTATDRDFGRNGIE RYELLQEPGGGGGGGSGGSRRAGAADSAPYPGGGGNGASGGGSGGSKRRLDASEGGG GTNPGGRSSVFELQVADTPDGEKQPQLIVKGALDREQRDSYELTLRVRDGGDPPRSS QAILRVLITDVNDNSPRFEKSVYEADLAENSAPGTPILQLRAADLDVGVNGQIEYVFGAA TESVRRLLRLDETSGWLSVLHRIDREEVNQLRFTVMARDRGQPPKTDKATVVLNIKDEN DNVPSIEIRKIGRIPLKDGVANVAEDVLVDTPIALVQVSDRDQGENGVVTCTVVGDVPFQ LKPASDTEGDQNKKKYFLHTSTPLDYEATREFNVVIVAVDSGSPSLSSKNSLIVKVGDTN DNPPMFGQSVVEVYFPENNIPGERVATVLATDADSGKNAEIAYSLDSSVMGIFAIDPDS GDILVNTVLDREQTDRYEFKVNAKDKGIPVLQGSTTVIVQVADKNDNDPKFMQDVFTFY VKENLQPNSPVGMVTVMDADKGRNAEMSLYIEENNNIFSIENDTGTIYSTMSFDREHQT TYTFRVKAVDGGDPPRSATATVSLFVMDENDNAPTVTLPKNISYTLLPPSSNVRTVVAT VLATDSDDGINADLNYSIVGGNPFKLFEIDPTSGVVSLVGKLTQKHYGLHRLVVQVNDS GQPSQSTTTVVHVFVNESVSNATAIDSQIARSLHIPLTQDIAGDPSYEISKQRLSIVIGVVA GIMTVILIILIVVMARYCRSKNKNGYEAGKKDHEDFFTPQQHDKSKKPKKDKKNKKSKQP LYSSIVTVEASKPNGQRYDSVNEKLSDSPSMGRYRSVNGGPGSPDLARHYKSSSPLPT VQLHPQSPTAGKKHQAVQDLPPANTFVGAGDNISIGSDHCSEYSCQTNNKYSKQMRLH **PYITVFG**

SEQID No:260

MEIGWMHNRRQRQVLVFFVLLSLSGAGAELGSYSVVEETERGSFVANLGKDLGLGLTE
MSTRKARIISQGNKQHLQLKAQTGDLLINEKLDREELCGPTEPCILHFQVLMENPLEIFQ
AELRVIDINDHSPMFTEKEMILKIPENSPLGTEFPLNHALDLDVGSNNVQNYKISPSSHFR
VLIHEFRDGRKYPELVLDKELDREEEPQLRLTLTALDGGSPPRSGTAQVRIEVVDINDNA
PEFEQPIYKVQIPENSPLGSLVATVSARDLDGGANGKISYTLFQPSEDISKTLEVNPMTG
EVRLRKQVDFEMVTSYEVRIKATDGGGLSGKCTLLLQVVDVNDNPPQVTMSALTSPIPE
NSPEIVVAVFSVSDPDSGNNGKTISSIQEDLPFLLKPSVKNFYTLVTERALDREARAEYNI
TLTVTDMGTPRLKTEHNITVQISDVNDNAPTFTQTSYTLFVRENNSPALHIGSVSATDRD
SGTNAQVTYSLLPPQDPHLPLASLVSINADNGHLFALRSLDYEALQAFEFRVGATDRGS
PALSREALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDS
GQNAWLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDAAKQRLVVLVKDNGEPPRS
ATATLHVLLVDGFSQPFLPLPEAAPGQTQANSLTVYLVVALASVSSLFLFSVLLFVAVRL
CRRSRAASVGRCSMPEGPFPGRLVDVSGTGTLSQSYQYEVCLTGGSETSEFKFLKPIIP
NFSP

MDEDVLTTLKILIIGESGVGKSSLLLRFTDDTFDPELAATIGVDFKVKTISVDGNKAKLAIW DTAGQERFRTLTPSYYRGAQGVILVYDVTRRDTFVKLDNWLNELETYCTRNDIVNMLVG NKIDKENREVDRNEGLKFARKHSMLFIEASAKTCDGVQCAFEELVEKIIQTPGLWESEN QNKGVKLSHREEGQGGGACGGYCSVL

SEQID No:262

MESRDHNNPQEGPTSSSGRRAAVEDNHLLIKAVQNEDVDLVQQLLEGGANVNFQEEE GGWTPLHNAVQMSREDIVELLLRHGADPVLRKKNGATPFILAAIAGSVKLLKLFLSKGAD VNECDFYGFTAFMEAAVYGKVKALKFLYKRGANVNLRRKTKEDQERLRKGGATALMDA AEKGHVEVLKILLDEMGADVNACDNMGRNALIHALLSSDDSDVEAITHLLLDHGADVNV RGERGKTPLILAVEKKHLGLVQRLLEQEHIEINDTDSDGKTALLLAVELKLKKIAELLCKR GASTDCGDLVMTARRNYDHSLVKVLLSHGAKEDFHPPAEDWKPQSSHWGAALKDLHR IYRPMIGKLKFFIDEKYKIADTSEGGIYLGFYEKQEVAVKTFCEGSPRAQREVSCLQSSR ENSHLVTFYGSESHRGHLFVCVTLCEQTLEACLDVHRGEDVENEEDEFARNVLSSIFKA VQELHLSCGYTHQDLQPQNILIDSKKAAHLADFDKSIKWAGDPQEVKRDLEDLGRLVLY VVKKGSISFEDLKAQSNEEVVQLSPDEETKDLIHRLFHPGEHVRDCLSDLLGHPFFWTW ESRYRTLRNVGNESDIKTRKSESEILRLLQPGPSEHSKSFDKWTTKINECVMKKMNKFY EKRGNFYQNTVGDLLKFIRNLGEHIDEEKHKKMKLKIGDPSLYFQKTFPDLVIYVYTKLQ NTEYRKHFPQTHSPNKPQCDGAGGASGLASPGC

SEQID No:263

MACSIVQFCYFQDLQAARDFLFPHLREEILSGALRRDPSKSTDWEDDGWGAWEENEP QEPEEGNTCKTQKTSWLQDCVLSLSPTNDLMVIAREQKAVFLVPKWKYSDKGKEEM QFAVGWSGSLNVEEGECVTSALCIPLASQKRSSTGRPDWTCIVVGFTSGYVRFYTENG VLLLAQLLNEDPVLQLKCRTYEIPRHPGVTEQNEELSILYPAAIVTIDGFSLFQSLRACRN QVAKAAASGNENIQPPPLAYKKWGLQDIDTIIDHASVGIMTLSPFDQMKTASNIGGFNAA IKNSPPAMSQYITVGSNPFTGFFYALEGSTQPLLSHVALAVASKLTSALFNAASGWLGW KSKHEEEAVQKQKPKVEPATPLAVRFGLPDSRRHGESICLSPCNTLAAVTDDFGRVILL DVARGIAIRMWKGYRDAQIGWIQTVEDLHERVPEKADFSPFGNSQGPSRVAQFLVIYAP RRGILEVWSTQQGPRVGAFNVGKHCRLLYPGYKIMGLNNVTSQSWQPQTYQICLVDPV SGSVKTVNVPFHLALSDKKSERAKDMHLVKKLAALLKTKSPNLDLVETEIKELILDIKYPA TKKQALESILASERLPFSCLRNITQTLMDTLKSQELESVDEGLLQFCANKLKLLQLYESVS QLNSLDFHLDTPFSDNDLALLLRLDEKELLKLQALLEKYKQENTRTNVRFSDDKDGVLP

VKTFLEYLEYEKDVLNIKKISEEEYVALGSFFFWKCLHGESSTEDMCHTLESAGLSPQLL
LSLLLSVWLSKEKDILDKPQSICCLHTMLSLLSKMKVAIDETWDSQSVSPWWQQMRTA
CIQSENNGAALLSAHVGHSVAAQISNNMTEKKFSQTVLGADSEALTDSWEALSLDTEY
WKLLLKQLEDCLILQTLLHSKGNTQTSKVSSLQAEPLPRLSVKKLLEGGKGGIADSVAK
WIFKQDFSPEVLKLANEERDAENPDEPKEGVNRSFLEVSEMEMDLGAIPDLLHLAYEQF
PCSLELDVLHAHCCWEYVVQWNKDPEEARFFVRSIEHLKQIFNAHVQNGIALMMWNTF
LVKRFSAATYLMDKVGKSPKDRLCRRDVGMSDTAMTSFLGSCLDLLQILMEADVSRDEI
QVPVLDTEDAWLSVEGPISIVELALEQKHIHYPLVEHHSILCSILYAVMRFSLKTVKPLSLF
DSKGKNAFFKDLTSIQLLPSGEMDPNFISVRQQFLLKVVSAAVQAQHSATKVKDPTEEA
TPTPFGKDQDWPALAVDLAHHLQVSEDVVRRHYVGELYNYGVDHLGEEAILQVHDKEV
LASQLLVLTGQRLAHALLHTQTKEGMELLARLPPTLCTWLKAMDPQDLQNTEVPIATTA
KLVNKVIELLPEKHGQYGLALHLIEAVEAISLPSL

SEQID No:264

MTVSGPGTPEPRPATPGASSVEQLRKEGNELFKCGDYGGALAAYTQALGLDATPQDQ AVLHRNRAACHLKLEDYDKAETEASKAIEKDGGDVKALYRRSQALEKLGRLDQAVLDLQ RCVSLEPKNKVFQEALRNIGGQIQEKVRYMSSTDAKVEQMFQILLDPEEKGTEKKQKAS QNLVVLAREDAGAEKIFRSNGVQLLQRLLDMGETDLMLAALRTLVGICSEHQSRTVATL SILGTRRVVSILGVESQAVSLAACHLLQVMFDALKEGVKKGFRGKEGAIIVDPARELKVLI SNLLDLLTEVGVSGQGRDNALTLLIKAVPRKSLKDPNNSLTLWVIDQGLKKILEVGGSLQ DPPGELAVTANSRMSASILLSKLFDDLKCDAERENFHRLCENYIKSWFEGQGLAGKLRA IQTVSCLLQGPCDAGNRALELSGVMESVIALCASEQEEEQLVAVEALIHAAGKAKRASFI TANGVSLLKDLYKCSEKDSIRIRALVGLCKLGSAGGTDFSMKQFAEGSTLKLAKQCRKW LCNDQIDAGTRRWAVEGLAYLTFDADVKEEFVEDAAALKALFQLSRLEERSVLFAVASA LVNCTNSYDYEEPDPKMVELAKYAKQHVPEQHPKDKPSFVRARVKKLLAAGVVSAMVC MVKTESPVLTSSCRELLSRVFLALVEEVEDRGTVVAQGGGRALIPLALEGTDVGQTKAA QALAKLTITSNPEMTFPGERIYEVVRPLVSLLHLNCSGLQNFEALMALTNLAGISERLRQ KILKEKAVPMIEGYMFEEHEMIRRAATECMCNLAMSKEVQDLFEAQGNDRLKLLVLYSG **EDDELLQRAAAGGLAMLTSMRPTLCSRIPQVTTHWLEILQALLLSSNQELQHRGAVVVL** NMVEASREIASTLMESEMMEILSVLAKGDHSPVTRAAAACLDKAVEYGLIQPNQDGE

SEQID No:265

MRPEPGGCCCRRTVRANGCVANGEVRNGYVRSSAAAAAAAAAGQIHHVTQNGGLYK RPFNEAFEETPMLVAVLTYVGYGVLTLFGYLRDFLRYWRIEKCHHATEREEQKDFVSLY QDFENFYTRNLYMRIRDNWNRPICSVPGARVDIMERQSHDYNWSFKYTGNIIKGVINMG SYNYLGFARNTGSCQEAAAKVLEEYGAGVCSTRQEIGNLDKHEELEELVARFLGVEAA MAYGMGFATNSMNIPALVGKGCLILSDELNHASLVLGARLSGATIRIFKHNNMQSLEKLL KDAIVYGQPRTRRPWKKILILVEGIYSMEGSIVRLPEVIALKKKYKAYLYLDEAHSIGALGP TGRGVVEYFGLDPEDVDVMMGTFTKSFGASGGYIGGKKELIDYLRTHSHSAVYATSLS PPVVEQIITSMKCIMGQDGTSLGKECVQQLAENTRYFRRRLKEMGFIIYGNEDSPVVPL MLYMPAKIGAFGREMLKRNIGVVVVGFPATPIIESRARFCLSAAHTKEILDTALKEIDEVG DLLQLKYSRHRLVPLLDRPFDETTYEETED

SEQID No:266

MSGELPPNINIKEPRWDQSTFIGRANHFFTVTDPRNILLTNEQLESARKIVHDYRQGIVP PGLTENELWRAKYIYDSAFHPDTGEKMILIGRMSAQVPMNMTITGCMMTFYRTTPAVLF WQWINQSFNAVVNYTNRSGDAPLTVNELGTAYVSATTGAVATALGLNALTKHVSPLIGR FVPFAAVAAANCINIPLMRQRELKVGIPVTDENGNRLGESANAAKQAITQVVVSRILMAA PGMAIPPFIMNTLEKKAFLKRFPWMSAPIQVGLVGFCLVFATPLCCALFPQKSSMSVTSL EAELQAKIQESHPELRRVYFNKGL

SEQID No:267

MSQWYELQQLDSKFLEQVHQLYDDSFPMEIRQYLAQWLEKQDWEHAANDVSFATIRF HDLLSQLDDQYSRFSLENNFLLQHNIRKSKRNLQDNFQEDPIQMSMIIYSCLKEERKILE NAQRFNQAQSGNIQSTVMLDKQKELDSKVRNVKDKVMCIEHEIKSLEDLQDEYDFKCK TLQNREHETNGVAKSDQKQEQLLLKKMYLMLDNKRKEVVHKIIELLNVTELTQNALINDE LVEWKRRQQSACIGGPPNACLDQLQNWFTIVAESLQQVRQQLKKLEELEQKYTYEHDP ITKNKQVLWDRTFSLFQQLIQSSFVVERQPCMPTHPQRPLVLKTGVQFTVKLRLLVKLQ ELNYNLKVKVLFDKDVNERNTVKGFRKFNILGTHTKVMNMEESTNGSLAAEFRHLQLKE QKNAGTRTNEGPLIVTEELHSLSFETQLCQPGLVIDLETTSLPVVVISNVSQLPSGWASIL WYNMLVAEPRNLSFFLTPPCARWAQLSEVLSWQFSSVTKRGLNVDQLNMLGEKLLGP NASPDGLIPWTRFCKENINDKNFPFWLWIESILELIKKHLLPLWNDGCIMGFISKERERAL LKDQQPGTFLLRFSESSREGAITFTWVERSQNGGEPDFHAVEPYTKKELSAVTFPDIIR NYKVMAAENIPENPLKYLYPNIDKDHAFGKYYSRPKEAPEPMELDGPKGTGYIKTELISV SEVHPSRLQTTDNLLPMSPEEFDEVSRIVGSVEFDSMMNTV

SEQID No:268

MEAVLNELVSVEDLLKFEKKFQSEKAAGSVSKSTQFEYAWCLVRTRYNDDIRKGIVLLE

ELLPKGSKEEQRDYVFYLAVGNYRLKEYEKALKYVRGLLQTEPQNNQAKELERLIDKAM KKDGLVGMAIVGGMALGVAGLAGLIGLAVSKSKS

SEQID No:269

MGAVARAHGGLRVARARESVAGGRHRGAGRPGARAAGAAAGLVRAEAGGRRAGRG
RRPGRGLPTGGGGLAAAAVGREVAQGLCDAIRLDGGLDLLLRLLQAPELETRVQAARL
LEQILVAENRDRVARIGLGVILNLAKEREPVELARSVAGILEHMFKHSEETCQRLVAAGG
LDAVLYWCRRTDPALLRHCALALGNCALHGGQAVQRRMVEKRAAEWLFPLAFSKEDE
LLRLHACLAVAVLATNKEVEREVERSGTLALVEPLVASLDPGRFARCLVDASDTSQGRG
PDDLQRLVPLLDSNRLEAQCIGAFYLCAEAAIKSLQGKTKVFSDIGAIQSLKRLVSYSTNG
TKSALAKRALRLLGEEVPRPILPSVPSWKEAEVQTWLQQIGFSKYCESFREQQVDGDLL
LRLTEEELQTDLGMKSGITRKRFFRELTELKTFANYSTCDRSNLADWLGSLDPRFRQYT
YGLVSCGLDRSLLHRVSEQQLLEDCGIHLGVHRARILTAAREMLHSPLPCTGGKPSGDT
PDVFISYRRNSGSQLASLLKVHLQLHGFSVFIDVEKLEAGKFEDKLIQSVMGARNFVLVL
SPGALDKCMQDHDCKDWVHKEIVTALSCGKNIVPIIDGFEWPEPQVLPEDMQAVLTFN
GIKWSHEYQEATIEKIIRFLQGRSSRDSSAGSDTSLEGAAPMGPT

SEQID No:270

MVGEEKMSLRNRLSKSRENPEEDEDQRNPAKESLETPSNGRIDIKQLIAKKIKLTAEAEE LKPFMKEVGSHFDDFVTNLIEKSASLDNGGCALTTFSVLEGEKNNHRAKDLRAPPEQG KIFIARRSLLDELLEVDHIRTIYHMFIALLILFILSTLVVDYIDEGRLVLEFSLLSYAFGKFPTV VWTWWIMFLSTFSVPYFLFQHWATGYSKSSHPLIRSLFHGFLFMIFQIGVLGFGPTYVVL AYTLPPASRFIIIFEQIRFVMKAHSFVRENVPRVLNSAKEKSSTVPIPTVNQYLYFLFAPTLI YRDSYPRNPTVRWGYVAMKFAQVFGCFFYVYYIFERLCAPLFRNIKQEPFSARVLVLCV FNSILPGVLILFLTFFAFLHCWLNAFAEMLRFGDRMFYKDWWNSTSYSNYYRTWNVVV HDWLYYYAYKDFLWFFSKRFKSAAMLAVFAVSAVVHEYALAVCLSFFYPVLFVLFMFFG MAFNFIVNDSRKKPIWNVLMWTSLFLGNGVLLCFYSQEWYARRHCPLKNPTFLDYVRP RSWTCRYVF

SEQID No:271

MKAMDVLPILKEKVAYLSGGRDKRGGPILTFPARSNHDRIRQEDLRRLISYLACIPSEEV CKRGFTVIVDMRGSKWDSIKPLLKILQESFPCCIHVALIIKPDNFWQKQRTNFGSSKFEF ETNMVSLEGLTKVVDPSQLTPEFDGCLEYNHEEWIEIRVAFEDYISNATHMLSRLEELQ DILAKKELPQDLEGARNMIEEHSQLKKKVIKAPIEDLDLEGQKLLQRIQSSESFPKKNSGS

GNADLQNLLPKVSTMLDRLHSTRQHLHQMWHVRKLKLDQCFQLRLFEQDAEKMFDWI THNKGLFLNSYTEIGTSHPHAMELQTQHNHFAMNCMNVYVNINRIMSVANRLVESGHY ASQQIRQIASQLEQEWKAFAAALDERSTLLDMSSIFHQKAEKYMSNVDSWCKACGEVD LPSELQDLEDAIHHHQGIYEHITLAYSEVSQDGKSLLDKLQRPLTPGSSDSLTASANYSK AVHHVLDVIHEVLHHQRHVRTIWQHRKVRLHQRLQLCVFQQEVQQVLDWIENHGEAFL SKHTGVGKSLHRARALQKRHEDFEEVAQNTYTNADKLLEAAEQLAQTGECDPEEIYQA AHQLEDRIQDFVRRVEQRKILLDMSVSFHTHVKELWTWLEELQKELLDDVYAESVEAVQ DLIKRFGQQQQTTLQVTVNVIKEGEDLIQQLRDSAISSNKTPHNSSINHIETVLQQLDEAQ SQMEELFQERKIKLELFLHVRIFERDAIDIISDLESWNDELSQQMNDFDTEDLTIAEQRLQ HHADKALTMNNLTFDVIHQGQDLLQYVNEVQASGVELLCDRDVDMATRVQDLLEFLHE KQQELDLAAEQHRKHLEQCVQLRHLQAEVKQVLGWIRNGESMLNAGLITASSLQEAEQ LQREHEQFQHAIEKTHQSALQVQQKAEAMLQANHYDMDMIRDCAEKVASHWQQLMLK MEDRLKLVNASVAFYKTSEQVCSVLESLEQEYKREEDWCGGADKLGPNSETDHVTPMI SKHLEQKEAFLKACTLARRNADVFLKYLHRNSVNMPGMVTHIKAPEQQVKNILNELFQR ENRVLHYWTMRKRRLDQCQQYVVFERSAKQALEWIHDNGEFYLSTHTSTGSSIQHTQ ELLKEHEEFQITAKQTKERVKLLIQLADGFCEKGHAHAAEIKKCVTAVDKRYRDFSLRME KYRTSLEKALGISSDSNKSSKSLQLDIIPASIPGSEVKLRDAAHELNEEKRKSARRKEFIM AELIQTEKAYVRDLRECMDTYLWEMTSGVEEIPPGIVNKELIIFGNMQEIYEFHNNIFLKE LEKYEQLPEDVGHCFVTWADKFQMYVTYCKNKPDSTQLILEHAGSYFDEIQQRHGLAN SISSYLIKPVQRITKYQLLLKELLTCCEEGKGEIKDGLEVMLSVPKRANDAMHLSMLEGF DENIESQGELILQESFQVWDPKTLIRKGRERHLFLFEMSLVFSKEVKDSSGRSKYLYKSK LFTSELGVTEHVEGDPCKFALWVGRTPTSDNKIVLKASSIENKQDWIKHIREVIQERTIHL KGALKEPIHIPKTAPATRQKGRRDGEDLDSQGDGSSQPDTISIASRTSQNTLDSDKLSG GCELTVVIHDFTACNSNELTIRRGQTVEVLERPHDKPDWCLVRTTDRSPAAEGLVPCGS LCIAHSRSSMEMEGIFNHKDSLSVSSNDASPPASVASLQPHMIGAQSSPGPKRPGNTL RKWLTSPVRRLSSGKADGHVKKLAHKHKKSREVRKSADAGSQKDSDDSAATPQDETV EERGRNEGLSSGTLSKSSSSGMQSCGEEEGEEGADAVPLPPPMAIQQHSLLQPDSQD DKASSRLLVRPTSSETPSAAELVSAIEELVKSKMALEDRPSSLLVDQGDSSSPSFNPSD NSLLSSSSPIDEMEERKSSSLKRRHYVLQELVETERDYVRDLGYVVEGYMALMKEDGV PDDMKGKDKIVFGNIHQIYDWHRDFFLGELEKCLEDPEKLGSLFVKHERRLHMYIAYCQ NKPKSEHIVSEYIDTFFEDLKQRLGHRLQLTDLLIKPVQRIMKYQLLLKDFLKYSKKASLD TSELERAVEVMCIVPRRCNDMMNVGRLQGFDGKIVAQGKLLLQDTFLVTDQDAGLLPR CRERRIFLFEQIVIFSEPLDKKKGFSMPGFLFKNSIKVSCLCLEENVENDPCKFALTSRTG DVVETFILHSSSPSVRQTWIHEINQILENQRNFLNALTSPIEYQRNHSGGGGGGGGGAA

AGVGAAAAAGPPVAAAATVAAPAAAAAPPARAGAGPPGSPSLSDTTPPCWSPLQPRA
RQRQTRCQSESSSSNISTMLVTHDYTAVKEDEINVYQGEVVQILASNQQNMFLVFRAA
TDQCPAAEGWIPGFVLGHTSAVIVENPDGTLKKSTSWHTALRLRKKSEKKDKDGKREG
KLENGYRKSREGLSNKVSVKLLNPNYIYDVPPEFVIPLSEVTCETGETVVLRCRVCGRP
KASITWKGPEHNTLNNDGHYSISYSDLGEATLKIVGVTTEDDGIYTCIAVNDMGSASSSA
SLRVLGPGMDGIMVTWKDNFDSFYSEVAELGRGRFSVVKKCDQKGTKRAVATKFVNK
KLMKRDQVTHELGILQSLQHPLLVGLLDTFETPTSYILVLEMADQGRLLDCVVRWGSLT
EGKIRAHLGEVLEAVRYLHNCRIAHLDLKPENILVDESLAKPTIKLADFGDAVQLNTTYYI
HQLLGNPEFAAPEIILGNPVSLTSDTWSVGVLTYVLLSGVSPFLDDSVEETCLNICRLDF
SFPDDYFKGVSQKAKEFVCFLLQEDPAKRPSAALALQEQWLQAGNGRSTGVLDTSRLT
SFIERRKHQNDVRPIRSIKNFLQSRLLPRV

SEQID No:272

MRKGLRATAARCGLGLGYLLQMLVLPALALLSASGTGSAAQDDDFFHELPETFPSDPP **EPLPHFLIEPEEAYIVKNKPVNLYCKASPATQIYFKCNSEWVHQKDHIVDERVDETSGLIV** REVSIEISRQQVEELFGPEDYWCQCVAWSSAGTTKSRKAYVRIAYLRKTFEQEPLGKEV SLEQEVLLQCRPPEGIPVAEVEWLKNEDIIDPVEDRNFYITIDHNLIIKQARLSDTANYTCV AKNIVAKRKSTTATVIVYVNGGWSTWTEWSVCNSRCGRGYQKRTRTCTNPAPLNGGA FCEGQSVQKIACTTLCPVDGRWTPWSKWSTCGTECTHWRRRECTAPAPKNGGKDCD GLVLQSKNCTDGLCMQTAPDSDDVALYVGIVIAVIVCLAISVVVALFVYRKNHRDFESDII DSSALNGGFQPVNIKAARQDLLAVPPDLTSAAAMYRGPVYALHDVSDKIPMTNSPILDP LPNLKIKVYNTSGAVSPQDDLSEFTSKLSPQMTQSLLENEALSLKNQSLARQTDPSCTA FGSFNSLGGHLIVPNSGVSLLIPAGAIPQGRVYEMYVTVHRKETMRPPMDDSQTLLTPV VSCGPPGALLTRPVVLTMHHCADPNTEDWKILLKNQAAQGQWEDVVVVGEENFTTPC YIKLDAEACHILTENLSTYALVGHSTTKAAAKRLKLAIFGPLCCSSLEYSIRVYCLDDTQD ALKEILHLERQTGGQLLEEPKALHFKGSTHNLRLSIHDIAHSLWKSKLLAKYQEIPFYHV WSGSQRNLHCTFTLERFSLNTVELVCKLCVRQVEGEGQIFQLNCTVSEEPTGIDLPLLD PANTITTVTGPSAFSIPLPIRQKLCSSLDAPQTRGHDWRMLAHKLNLDRYLNYFATKSSP TGVILDLWEAQNFPDGNLSMLAAVLEEMGRHETVVSLAAEGQY

SEQID No:273

MAVFVVLLALVAGVLGNEFSILKSPGSVVFRNGNWPIPGERIPDVAALSMGFSVKEDLS WPGLAVGNLFHRPRATVMVMVKGVNKLALPPGSVISYPLENAVPFSLDSVANSIHSLFS EETPVVLQLAPSEERVYMVGKANSVFEDLSVTLRQLRNRLFQENSVLSSLPLNSLSRNN

EVDLLFLSELQVLHDISSLLSRHKHLAKDHSPDLYSLELAGLDEIGKRYGEDSEQFRDAS KILVDALQKFADDMYSLYGGNAVVELVTVKSFDTSLIRKTRTILEAKRAKNPASPYNLAY KYNFEYSVVFNMVLWIMIALALAVIITSYNIWNMDPGYDSIIYRMTNQKIRMD

SEQID No:274

MTFYLFGIRSFPKLWKSPYLGLGPGHSYVSLFLADRCGIRNQQRLFSLKTMSPQNTKAT NLIAKARYLRKDEGSNKQVYSVPHFFLAGAAKERSQMNSQTEDHALAPVRNTIQLPTQP LNSEEWDKLKEDLKENTGKTSFESWIISQMAGCHSSIDVAKSLLAWVAAKNNGIVSYDL LVKYLYLCVFHMQTSEVIDVFEIMKARYKTLEPRGYSLLIRGLIHSDRWREALLLLEDIKK VITPSKKNYNDCIQGALLHQDVNTAWNLYQELLGHDIVPMLETLKAFFDFGKDIKDDNYS NKLLDILSYLRNNQLYPGESFAHSIKTWFESGQCSGCGKTIESIQLSPEEYECLKGKIMR DVIDGGDQYRKTTPQELKRFENFIKSRPPFDVVIDGLNVAKMFPKVRESQLLLNVVSQL AKRNLRLLVLGRKHMLRRSSQWSRDEMEEVQKQASCFFADDISEDDPFLLYATLHSGN HCRFITRDLMRDHKACLPDAKTQRLFFKWQQGHQLAIVNRFPGSKLTFQRILSYDTVVQ TTGDSWHIPYDEDLVERCSCEVPTKWLCLHQKT

SEQID No:275

MALALAALAAVEPACGSRYQQLQNEEESGEPEQAAGDAPPPYSSISAESAAYFDYKDE SGFPKPPSYNVATTLPSYDEAERTKAEATIPLVPGRDEDFVGRDDFDDADQLRIGNDGI FMLTFFMAFLFNWIGFFLSFCLTTSAAGRYGAISGFGLSLIKWILIVRFSTYFPGYFDGQY WLWWVFLVLGFLLFLRGFINYAKVRKMPETFSNLPRTRVLFIY

SEQID No:276

MDPECAQLLPALCAVLVDPGQPVADDTCLEKLLDWFKTVTEGESSVVLLQEHPCLVELL SHVLKVQDLSSGVLSFSLRLAGTFAAQENCFQYLQQGELLPGLFGEPGPLGRATWAVP TVRSGWIQGLRSLAQHPSALRFLADHGAVDTIFSLQGDSSLFVASAASQLLVHVLALSM RGGAEGQPCLPGGDWPACAQKIMDHVEESLCSAATPKVTQALNVLTTTFGRCQSPWT EALWVRLSPRVACLLERDPIPAAHSFVDLLLCVARSPVFSSSDGSLWETVARALSCLGP THMGPLALGILKLEHCPQALRTQAFQVLLQPLACVLKATVQAPGPPGLLDGTADDATTV DTLLASKSSCAGLLCRTLAHLEELQPLPQRPSPWPQASLLGATVTVLRLCDGSAAPASS VGGHLCGTLAGCVRVQRAALDFLGTLSQGTGPQELVTQALAVLLECLESPGSSPTVLK KAFQATLRWLLSSPKTPGCSDLGPLIPQFLRELFPVLQKRLCHPCWEVRDSALEFLTQL SRHWGGQADFRCALLASEVPQLALQLLQDPESYVRASAVTAMGQLSSQGLHAPTSPE HAEARQSLFLELLHILSVDSEGFPRRAVMQVFTEWLRDGHADAAQDTEQFVATVLQAA

SRDLDWEVRAQGLELALVFLGQTLGPPRTHCPYAVALPEVAPAQPLTEALRALCHVGL
FDFAFCALFDCDRPVAQKSCDLLLFLRDKIASYSSLREARGSPNTASAEATLPRWRAGE
QAQPPGDQEPEAVLAMLRSLDLEGLRSTLAESSDHVEKSPQSLLQDMLATGGFLQGDE
ADCY

SEQID No:277

MVNYAWAGRSQRKLWWRSVAVLTCKSVVRPGYRGGLQARRSTLLKTCARARATAPG AMKMVAPWTRFYSNSCCLCCHVRTGTILLGVWYLIINAVVLLILLSALADPDQYNFSSSE LGGDFEFMDDANMCIAIAISLLMILICAMATYGAYKQRAAWIIPFFCYQIFDFALNMLVAIT VLIYPNSIQEYIRQLPPNFPYRDDVMSVNPTCLVLIILLFISIILTFKGYLISCVWNCYRYING RNSSDVLVYVTSNDTTVLLPPYDDATVNGAAKEPPPPYVSA

SEQID No:278

MNIFDRKINFDALLKFSHITPSTQQHLKKVYASFALCMFVAAAGAYVHMVTHFIQAGLLS ALGSLILMIWLMATPHSHETEQKRLGLLAGFAFLTGVGLGPALEFCIAVNPSILPTAFMGT AMIFTCFTLSALYARRRSYLFLGGILMSALSLLLLSSLGNVFFGSIWLFQANLYVGLVVMC GFVLFDTQLIIEKAEHGDQDYIWHCIDLFLDFITVFRKLMMILAMNEKDKKKEKK

SEQID No:279

MASILDEYENSLSRSAVLQPGCPSVGIPHSGYVNAQLEKEVPIFTKQRIDFTPSERITSLV VSSNQLCMSLGKDTLLRIDLGKANEPNHVELGRKDDAKVHKMFLDHTGSHLLIALSSTE VLYVNRNGQKVRPLARWKGQLVESVGWNKALGTESSTGPILVGTAQGHIFEAELSASE GGLFGPAPDLYFRPLYVLNEEGGPAPVCSLEAERGPDGRSFVIATTRQRLFQFIGRAAE GAEAQGFSGLFAAYTDHPPPFREFPSNLGYSELAFYTPKLRSAPRAFAWMMGDGVLY GALDCGRPDSLLSEERVWEYPEGVGPGASPPLAIVLTQFHFLLLLADRVEAVCTLTGQV VLRDHFLEKFGPLKHMVKDSSTGQLWAYTERAVFRYHVQREARDVWRTYLDMNRFDL AKEYCRERPDCLDTVLAREADFCFRQRRYLESARCYALTQSYFEEIALKFLEARQEEAL AEFLQRKLASLKPAERTQATLLTTWLTELYLSRLGALQGDPEALTLYREVRNLTQFHPLP LAPLLSLSFPTHVLFTSREREREHLSSVCSLCGLWNPSSSLSEEAFSSSCL

SEQID No:280

MTSATSPIILKWDPKSLEIRTLTVERLLEPLVTQVTTLVNTSNKGPSGKKKGRSKKAHVL AASVEQATQNFLEKGEQIAKESQDLKEELVAAVEDVRKQGETMRIASSEFADDPCSSVK RGTMVRAARALLSAVTRLLILADMADVMRLLSHLKIVEEALEAVKNATNEQDLANRFKEF GKKMVKLNYVAARRQQELKDPHCRDEMAAARGALKKNATMLYTASQAFLRHPDVAAT RANRDYVFKQVQEAIAGISNAAQATSPTDEAKGHTGIGELAAALNEFDNKIILDPMTFSE ARFRPSLEERLESIISGAALMADSSCTRDDRRERIVAECNAVRQALQDLLSEYMNNTGR KEKGDPLNIAIDKMTKKTRDLRRQLRKAVMDHISDSFLETNVPLLVLIEAAKSGNEKEVK EYAQVFREHANKLVEVANLACSISNNEEGVKLVRMAATQIDSLCPQVINAALTLAARPQS KVAQDNMDVFKDQWEKQVRVLTEAVDDITSVDDFLSVSENHILEDVNKCVIALQEGDVD TLDRTAGAIRGRAARVIHIINAEMENYEAGVYTEKVLEATKLLSETVMPRFAEQVEVAIEA LSANVPQPFEENEFIDASRLVYDGVRDIRKAVLMIRTPEELEDDSDFEQEDYDVRRGTS VQTEDDQLIAGQSARAIMAQLPQEEKAKIAEQVEIFHQEKSKLDAEVAKWDDSGNDIIVL AKQMCMIMMEMTDFTRGKGPLKNTSDVINAAKKIAEAGSRMDKLARAVADQCPDSACK QDLLAYLQRIALYCHQLNICSKVKAEVQNLGGELIVSGTGVQSTFTTFYEVDCDVIDGGR ASQLSTHLPTCAEGAPIGSGSSDSSMLDSATSLIQAAKNLMNAVVLTVKASYVASTKYQ KVYGTAAVNSPVVSWKMKAPEKKPLVKREKPEEFQTRVRRGSQKKHISPVQALSEFKA MDSF

SEQID No:281

MSGDSERAVAPGVVPAPCASKVELRLSCRHLLDRDPLTKSDPSVVLLQQAQGQWLQVDRTEVVKSSLHPVFSKVFTVDYYFEGVQKLRFEVYDTHGPSGLTCQDDDFLGGMECTLGQIVAQKKMTRPLLLRFGRNAGKSTITVIAEDISGNNGYVELSFQARKLDDKDLFSKSDPFLELYRVNDDGSEQLVYRTEVVKNNLNPVWEPFKVSLNSLCSCEETRPLKCLVWDYDSRGKHDFIGDFTTTFAEMQKAFEEEQQAQWDCVNAKYKQKKRNYKNSGVVILADLKLHRVHSFLDYIMGGCQIHCTVAIDFTASNGDPRNSCSLHHINPYQPNEYLRALVAVGEVCQDYDSDKRFSALGFGARIPPKYEVSHDFAINFNPEDDECEGIQGVVEAYQNCLPKVQLYGPTNVAPIISKVARMAAAEESTGEASQYYILLILTDGVVTDMSDTREAIVRASHLPMSVIIVGVGNADFTDMQILDGDDGVLRSPRGEPALRDIVQFVPFRELKNASPAALAKCVLAEVPKQVVEYYSHKELPPRSLGAQTGEAAASSAP

SEQID No:282

MAAQCVTKVALNVSCANLLDKDIGSKSDPLCVLFLNTSGQQWYEVERTERIKNCLNPQF SKTFIIDYYFEVVQKLKFGVYDIDNKTIELSDDDFLGECECTLGQIVSSKKLTRPLVMKTG RPAGKGSITISAEEIKDNRVVLFEMEARKLDNKDLFGKSDPYLEFHKQTSDGNWLMVHR TEVVKNNLNPVWRPFKISLNSLCYGDMDKTIKVECYDYDNDGSHDLIGTFQTTMTKLKE ASRSSPVEFECINEKKRQKKKSYKNSGVISVKQCEITVECTFLDYIMGGCQLNFTVGVDF TGSNGDPRSPDSLHYISPNGVNEYLTALWSVGLVIQDYDADKMFPAFGFGAQIPPQWQ VSHEFPMNFNPSNPYCNGIQGIVEAYRSCLPQIKLYGPTNFSPIINHVARFAAAATQQQT ASQYFVLLIITDGVITDLDETRQAIVNASRLPMSIIIVGVGGADFSAMEFLDGDGGSLRSPL GEVAIRDIVQFVPFRQFQNAPKEALAQCVLAEIPQQVVGYFNTYKLLPPKNPATKQQKQ

SEQID No:283

MAVSASPVISATSSGAGVPGGLFRAEPLYSTPREPPRLTPNMINSFVVNNHSNSAGGG
GRGNTNTNECRMVDMHGMKVASFLMDGQELICLPQVFDLFLKHLVGGLHTVYTKLKRL
DISPVVCTVEQVRILRGLGAIQPGVNRCKLITRKDFETLFTDCTNARRKRQMTRKQAVN
SSRPGRPPKRSLGVLQENARLLTHAVPGLLSPGLITPTGITAAAMAEAMKLQKMKLMAM
NTLQGNGSQNGTESEPDDLNSNTGGSESSWDKDKMQSPFAAPGPQHGIAHAALAGQ
PGIGGAPTLNPLQQNHLLTNRLDLPFMMMPHPLLPVSLPPASVAMAMNQMNHLNTIAN
MAAAAQIHSPLSRAGTSVIKERIPESPSPAPSLEENHRPGSQTSSHTSSSVSSSPSQMD
HHLERMEEVPVQIPIMKSPLDKIQLTPGQALPAGFPGPFIFADSLSSVETLLTNIQGLLKV
ALDNARIQEKQIQQEKKELRLELYREREIRENLERQLAVELQSRTTMQKRLKKEKKTKRK
LQEALEFESKRREQVEQALKQATTSDSGLRMLKDTGIPDIEIENNGTPHDSAAMQGGNY
YCLEMAQQLYSA

SEQID No:284

MDDSEVESTASILASVKEQEAQFEKLTRALEEERRHVSAQLERVRVSPQDANPLMANG TLTRRHQNGRFVGDADLERQKFSDLKLNGPQDHSHLLYSTIPRMQEPGQIVETYTEED PEGAMSVVSVETSDDGTTRRTETTVKKVVKTVTTRTVQPVAMGPDGLPVDASSVSNNY IQTLGRDFRKNGNGGPGPYVGQAGTATLPRNFHYPPDGYSRHYEDGYPGGSDNYGSL SRVTRIEERYRPSMEGYRAPSRQDVYGPQPQVRVGGSSVDLHRFHPEPYGLEDDQRS MGYDDLDYGMMSDYGTARRTGTPSDPRRRLRSYEDMIGEEVPSDQYYWAPLAQHER GSLASLDSLRKGGPPPPNWRQPELPEVIAMLGFRLDAVKSNAAAYLQHLCYRNDKVKT DVRKLKGIPŶLVGLLDHPKKEVHLGACGALKNISFGRDQDNKIAIKNCDGVPALVRLLRK ARDMDLTEVITGTLWNLSSHDSIKMEIVDHALHALTDEVIIPHSGWEREPNEDCKPRHIE WESVLTNTAGCLRNVSSERSEARRKLRECDGLVDALIFIVQAEIGQKDSDSKLVENCVC LLRNLSYQVHREIPQAERYQEAAPNVANNTGPHAASCFGAKKGKGKKPIEDPANDTVD FPKRTSPARGYELLFQPEVVRIYISLLKESKTPAILEASAGAIQNLCAGRWTYGRYIRSAL RQEKALSAIADLLTNEHERVVKAASGALRNLAVDARNKELIGKHAIPNLVKNLPGGQQN SSWNFSEDTVISILNTINEVIAENLEAAKKLRETQGIEKLVLINKSGNRSEKEVRAAALVLQ TIWGYKELRKPLEKEGWKKSDFQVNLNNASRSQSSHSYDDSTLPLIDRNQKSDNNYST

PNERGDHNRTLDRSGDLGDMEPLKGTTPLMQDEGQESLEEELDVLVLDDEGGQVSYP SMQKI

SEQID No:285

MACPALGLEALQPLQPEPPPEPAFSEAQKWIEQVTGRSFGDKDFRTGLENGILLCELLN AIKPGLVKKINRLPTPIAGLDNIILFLRGCKELGLKESQLFDPSDLQDTSNRVTVKSLDYSR KLKNVLVTIYWLGKAANSCTSYSGTTLNLKEFEGLLAQMRKDTDDIESPKRSIRDSGYID CWDSERSDSLSPPRHGRDDSFDSLDSFGSRSRQTPSPDVVLRGSSDGRGSDSESDLP HRKLPDVKKDDMSARRTSHGEPKSAVPFNQYLPNKSNQTAYVPAPLRKKKAEREEYR KSWSTATSPLGGERPFRYGPRTPVSDDAESTSMFDMRCEEEAAVQPHSRARQEQLQL INNQLREEDDKWQDDLARWKSRRRSVSQDLIKKEEERKKMEKLLAGEDGTSERRKSIK **TYREIVQEKERRERELHEAYKNARSQEEAEGILQQYIERFTISEAVLERLEMPKILERSHS** TEPNLSSFLNDPNPMKYLRQQSLPPPKFTATVETTIARASVLDTSMSAGSGSPSKTVTP KAVPMLTPKPYSQPKNSQDVLKTFKVDGKVSVNGETVHREEEKERECPTVAPAHSLTK SQMFEGVARVHGSPLELKQDNGSIEINIKKPNSVPQELAATTEKTEPNSQEDKNDGGKS RKGNIELASSEPQHFTTTVTRCSPTVAFVEFPSSPQLKNDVSEEKDQKKPENEMSGKV ELVLSQKVVKPKSPEPEATLTFPFLDKMPEANQLHLPNLNSQVDSPSSEKSPVMTPFKF WAWDPEEERRRQEKWQQEQERLLQERYQKEQDKLKEEWEKAQKEVEEEERRYYEE **ERKIIEDTVVPFTVSSSSADQLSTSSSMTEGSGTMNKIDLGNCQDEKQDRRWKKSFQG** DDSDLLLKTRESDRLEEKGSLTEGALAHSGNPVSKGVHEDHQLDTEAGAPHCGTNPQL AQDPSQNQQTSNPTHSSEDVKPKTLPLDKSINHQIESPSERRKKSPREHFQAGPFSPC SPTPPGQSPNRSISGKKLCSSCGLPLGKGAAMIIETLNLYFHIQCFRCGICKGQLGDAVS **GTDVRIRNGLLNCNDCYMRSRSAGQPTTL**

SEQID No:286

MAARGRRAEPQGREAPGPAGGGGGGSRWAESGSGTSPESGDEEVSGAGSSPVSGG VNLFANDGSFLELFKRKMEEEQRQRQEEPPPGPQRPDQSAAAAGPGDPKRKGGPGS TLSFVGKRRGGNKLALKTGIVAKKQKTEDEVLTSKGDAWAKYMAEVKKYKAHQCGDD DKTRPLVK

SEQID No:287

MAAETQTLNFGPEWLRALSSGGSITSPPLSPALPKYKLADYRYGREEMLALFLKDNKIP SDLLDKEFLPILQEEPLPPLALVPFTEEEQRNFSMSVNSAAVLRLTGRGGGGTVVGAPR GRSSSRGRGRGGCGFYQRSFDEVEGVFGRGGGREMHRSQSWEERGDRRFEKP GRKDVGRPNFEEGGPTSVGRKHEFIRSESENWRIFREEQNGEDEDGGWRLAGSRRD GERWRPHSPDGPRSAGWREHMERRRRFEFDFRDRDDERGYRRVRSGSGSIDDDRD SLPEWCLEDAEEEMGTFDSSGAFLSLKKVQKEPIPEEQEMDFRPVDEGEECSDSEGSH NEEAKEPDKTNKKEGEKTDRVGVEASEETPQTSSSSARPGTPSDHQSQEASQFERKD **EPKTEQTEKAEEETRMENSLPAKVPSRGDEMVADVQQPLSQIPSDTASPLLILPPPVPN PSPTLRPVETPVVGAPGMGSVSTEPDDEEGLKHLEQQAEKMVAYLQDSALDDERLASK** LQEHRAKGVSIPLMHEAMQKWYYKDPQGEIQGPFNNQEMAEWFQAGYFTMSLLVKRA CDESFQPLGDIMKMWGRVPFSPGPAPPPHMGELDQERLTRQQELTALYQMQHLQYQ QFLIQQQYAQVLAQQQKAALSSQQQQQLALLLQQFQTLKMRISDQNIIPSVTRSVSVPD TGSIWELQPTASQPTVWEGGSVWDLPLDTTTPGPALEQLQQLEKAKAAKLEQERREAE MRAKREEEERKRQEELRRQQEEILRRQQEEERKRREEEELARRKQEEALRRQREQEIA LRRQREEEERQQQEEALRRLEERRREEEERRKQEELLRKQEEEAAKWAREEEEAQRR LEENRLRMEEEAARLRHEEEERKRKELEVQRQKELMRQRQQQQEALRRLQQQQQQQ QLAQMKLPSSSTWGQQSNTTACQSQATLSLAEIQKLEEERERQLREEQRRQQRELMK ALQQQQQQQQKLSGWGNVSKPSGTTKSLLEIQQEEARQMQKQQQQQQQQQHQQPNR ARNNTHSNLHTSIGNSVWGSINTGPPNQWASDLVSSIWSNADTKNSNMGFWDDAVKE VGPRNSTNKNKKELK

SEQID No:288

MVGKLKQNLLLACLVISSVTVFYLGQHAMECHHRIEERSQPVKLESTRTTVRTGLDLKA NKTFAYHKDMPLIFIGGVPRSGTTLMRAMLDAHPDIRCGEETRVIPRILALKQMWSRSSK EKIRLDEAGVTDEVLDSAMQAFLLEIIVKHGEPAPYLCNKDPFALKSLTYLSRLFPNAKFL LMVRDGRASVHSMISRKVTIAGFDLNSYRDCLTKWNRAIETMYNQCMEVGYKKCMLVH YEQLVLHPERWMRTLLKFLQIPWNHSVLHHEEMIGKAGGVSLSKVERSTDQVIKPVNV GALSKWVGKIPPDVLQDMAVIAPMLAKLGYDPYANPPNYGKPDPKIIENTRRVYKGEFQ LPDFLKEKPQTEQVE

SEQID No:289

MSTFRQEDVEDHYEMGEELGSGQFAIVRKCRQKGTGKEYAAKFIKKRRLSSSRRGVSR EEIEREVNILREIRHPNIITLHDIFENKTDVVLILELVSGGELFDFLAEKESLTEDEATQFLK QILDGVHYLHSKRIAHFDLKPENIMLLDKNVPNPRIKLIDFGIAHKIEAGNEFKNIFGTPEF VAPEIVNYEPLGLEADMWSIGVITYILLSGASPFLGETKQETLTNISAVNYDFDEEYFSNT SELAKDFIRRLLVKDPKRRMTIAQSLEHSWIKAIRRRNVRGEDSGRKPERRRLKTTRLKE YTIKSHSSLPPNNSYADFERFSKVLEEAAAAEEGLRELQRSRRLCHEDVEALAAIYEEKE AWYREESDSLGQDLRRLRQELLKTEALKRQAQEEAKGALLGTSGLKRRFSRLENRYEA LAKQVASEMRFVQDLVRALEQEKLQGVECGLR

SEQID No:290

MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPS GTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPC GIDKFRGVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEE EEVAEVEEEADDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTESVEEVVRVP TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKN LPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQ AVPPRPHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE RMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISYGNDALMPSLT ETKTTVELLPVNGEFSLDDLQPWHSFGADSVPANTENEVEPVDARPAADRGLTTRPGS GLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIV ITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

SEQID No:291

SEQID No:292

RHTRTHRDTRHTYTHAHTDAHTCTHMHRDTQMHTHTICRKKYALTNIQAAMGLSDPAA QPLLGNGSANIKLVKNGENQLRKAAEQGQQDPNKNLSPTAVINITSEKLEGKEPHPQDS SSCEILPSQPRRTKSFLNYYADLETSARELEQNRGNHHGTAEEKSQPVQGQASTIIGNG DLLLQKPNRPQSSPEDGQVATVSSSPETKKDHPKTGAKTDCALHRIQNLAPSDEESSW TTLSQDSASPSSPDETDIWSDHSFQTDPDLPPGWKRVSDIAGTYYWHIPTGTTQWERP

VSIPADLQGSRKGSLSSVTPSPTPENEKQPWSDFAVLNGGKINSDIWKDLHAATVNPDP SLKEFEGATLRYASLKLRNAPHPDDDDSCSINSDPEAKCFAVRSLGWVEMAEEDLAPG KSSVAVNNCIRQLSYCKNDIRDTVGIWGEGKDMYLILENDMLSLVDPMDRSVWHSQPIV SIRVWGVGRDNGRDFAYVARDKDTRILKCHVFRCDTPAKAIATSLHEICSKIMAERKNAK ALACSSLQERANVNLDVPLQVDFPTPKTELVQKFHVQYLGMLPVDKPVGMDILNSAIEN LMTSSNKEDWLSVNMNVADATVTVISEKNEEEVLVECRVRFLSFMGVGKDVHTFAFIM DTGNQRFECHVFWCEPNAGNVSEAVQAACMLRYQKCLVARPPSQKVRPPPPPADSV TRRVTTNVKRGVLSLIDTLKQKRPVTEMP

SEQID No:293

MAQVAMSTLPVEDEESSESRMVVTFLMSALESMCKELAKSKAEVACIAVYETDVFVVG TERGRAFVNTRKDFQKDFVKYCVEEEEKAAEMHKMKSTTQANRMSVDAVEIETLRKTV **EDYFCFCYGKALGKSTVVPVPYEKMLRDQSAVVVQGLPEGVAFKHPENYDLATLKWIL ENKAGISFIIKRPFLEPKKHVGGRVMVTDADRSILSPGGSCGPIKVKTEPTEDSGISLEMA** AVTVKEESEDPDYYQYNIQAGPSETDDVDEKQPLSKPLQGSHHSSEGNEGTEMEVPA EDSTQHVPSETSEDPEVEVTIEDDDYSPPSKRPKANELPQPPVPEPANAGKRKVREFN FEKWNARITDLRKQVEELFERKYAQAIKAKGPVTIPYPLFQSHVEDLYVEGLPEGIPFRR PSTYGIPRLERILLAKERIRFVIKKHELLNSTREDLQLDKPASGVKEEWYARITKLRKMVD QLFCKKFAEALGSTEAKAVPYQKFEAHPNDLYVEGLPENIPFRSPSWYGIPRLEKIIQVG NRIKFVIKRPELLTHSTTEVTQPRTNTPVKEDWNVRITKLRKQVEEIFNLKFAQALGLTEA VKVPYPVFESNPEFLYVEGLPEGIPFRSPTWFGIPRLERIVRGSNKIKFVVKKPELVISYL PPGMASKINTKALQSPKRPRSPGSNSKVPEIEVTVEGPNNNNPQTSAVRTPTQTNGSN VPFKPRGREFSFEAWNAKITDLKQKVENLFNEKCGEALGLKQAVKVPFALFESFPEDFY VEGLPEGVPFRRPSTFGIPRLEKILRNKAKIKFIIKKPEMFETAIKESTSSKSPPRKINSSP NVNTTASGVEDLNIIQVTIPDDDNERLSKVEKARQLREQVNDLFSRKFGEAIGMGFPVKV PYRKITINPGCVVVDGMPPGVSFKAPSYLEISSMRRILDSAEFIKFTVIRPFPGLVINNQLV DQSESEGPVIQESAEPSQLEVPATEEIKETDGSSQIKQEPDPTW

SEQID No:294

MAFVCLAIGCLYTFLISTTFGCTSSSDTEIKVNPPQDFEIVDPGYLGYLYLQWQPPLSLD HFKECTVEYELKYRNIGSETWKTIITKNLHYKDGFDLNKGIEAKIHTLLPWQCTNGSEVQ SSWAETTYWISPQGIPETKVQDMDCVYYNWQYLLCSWKPGIGVLLDTNYNLFYWYEGL DHALQCVDYIKADGQNIGCRFPYLEASDYKDFYICVNGSSENKPIRSSYFTFQLQNIVKP LPPVYLTFTRESSCEIKLKWSIPLGPIPARCFDYEIEIREDDTTLVTATVENETYTLKTTNE

TRQLCFVVRSKVNIYCSDDGIWSEWSDKQCWEGEDLSKKTLLRFWLPFGFILILVIFVTG LLLRKPNTYPKMIPEFFCDT

SEQID No:295

MAERESGGLGGGAASPPAASPFLGLHIASPPNFRLTHDISLEEFEDEDLSEITDECGISL QCKDTLSLRPPRAGLLSAGGGGAGSRLQAEMLQMDLIDATGDTPGAEDDEEDDDEER AARRPGAGPPKAESGQEPASRGQGQSQGQSQGPGSGDTYRPKRPTTLNLFPQVPRS QDTLNNNSLGKKHSWQDRVSRSSSPLKTGEQTPPHEHICLSDELPPQSGPAPTTDRGT STDSPCRRSTATQMAPPGGPPAAPPGGRGHSHRDRIHYQADVRLEATEEIYLTPVQRP PDAAEPTSAFLPPTESRMSVSSDPDPAAYPSTAGRPHPSISEEEEGFDCLSSPERAEPP GGGWRGSLGEPPPPPRASLSSDTSALSYDSVKYTLVVDEHAQLELVSLRPCFGDYSDE SDSATVYDNCASVSSPYESAIGEEYEEAPRPQPPACLSEDSTPDEPDVHFSKKFLNVF MSGRSRSSSAESFGLFSCIINGEEQEQTHRAIFRFVPRHEDELELEVDDPLLVELQAED YWYEAYNMRTGARGVFPAYYAIEVTKEPEHMAALAKNSDWVDQFRVKFLGSVQVPYH KGNDVLCAAMQKIATTRRLTVHFNPPSSCVLEISVRGVKIGVKADDSQEAKGNKCSHFF QLKNISFCGYHPKNNKYFGFITKHPADHRFACHVFVSEDSTKALAESVGRAFQQFYKQF VEYTCPTEDIYLE

SEQID No:296

GSELETAMETLINVFHAHSGKEGDKYKLSKKELKELLQTELSGFLDAQKDVDAVDKVMK ELDENGDGEVDFQEYVVLVAALTVACNNFFWENS

SEQID No:297

MASTTTCTRFTDEYQLFEELGKGAFSVVRRCMKIPTGQGYAAKIINTKKLSARDHQKLE REARICRLLKHPNIVRLHDSISEEGFHYLVFDLVTGGELFEDIVAREYYSEADASHCIQQI LESVNHCHLNGIVHRDLKPENLLLASKSKGAAVKLADFGLAIEVQGDQQAWFGFAGTP GYLSPEVLRKDPYGKPVDMWACGVILYILLVGYPPFWDEDQHRLYQQIKAGAYDFPSP EWDTVTPEAKDLINKMLTINPAKRITASEALKHPWICQRSTVASMMHRQETVDCLKKFN ARRKLKGAILTTMLATRNFSAAKSLLKKPDGVKESTESSNTTIEDEDVKARKQEIIKVTEQ LIEAINNGDFEAYTKICDPGLTAFEPEALGNLVEGMDFHRFYFENALSKSNKPIHTIILNPH VHLVGDDAACIAYIRLTQYMDGSGMPKTMQSEETRVWHRRDGKWQNVHFHRSGSPT VPIKPPCIPNGKENFSGGTSLWQNI

SEQID No:298

MTATEALLRVLLLLAFGHSTYGAECFPACNPQNGFCEDDNVCRCQPGWQGPLCDQC VTSPGCLHGLCGEPGQCICTDGWDGELCDRDVRACSSAPCANNGTCVSLDGGLYECS CAPGYSGKDCQKKDGPCVINGSPCQHGGTCVDDEGRASHASCLCPPGFSGNFCEIVA NSCTPNPCENDGVCTDIGGDFRCRCPAGFIDKTCSRPVTNCASSPCQNGGTCLQHTQ VSYECLCKPEFTGLTCVKKRALSPQQVTRLPSGYGLAYRLTPGVHELPVQQPEHRILKV SMKELNKKTPLLTEGQAICFTILGVLTSLVVLGTVGIVFLNKCETWVSNLRYNHMLRKKK NLLLQYNSGEDLAVNIIFPEKIDMTTFSKEAGDEEI

SEQID No:299

MATIPDWKLQLLARRRQEEASVRGREKAERERLSQMPAWKRGLLERRRAKLGLSPGE PSPVLGTVEAGPPDPDESAVLLEAIGPVHQNRFIRQERQQQQQQQQQRSEELLAERKPG PLEARERRPSPGEMRDQSPKGRESREERLSPRETRERRLGIGGAQELSLRPLEARDW RQSPGEVGDRSSRLSEAWKWRLSPGETPERSLRLAESREQSPRRKEVESRLSPGESA YQKLGLTEAHKWRPDSRESQEQSLVQLEATEWRLRSGEERQDYSEECGRKEEWPVPGVAPKETAELSETLTREAQGNSSAGVEAAEQRPVEDGERGMKPTEGWKWTLNSGKA REWTPRDIEAQTQKLEPPESAEKLLESPGVEAGEGEAEKEEAGAQGRPLRALQNCCSVPSPLPPEDAGTGGLRQQEEEAVELQPPPPAPLSPPPPAPTAPQPPGDPLMSRLFYGVKAGPGVGAPRRSGHTFTVNPRRSVPPATPATPTSPATVDAAVPGAGKKRYPTAEEILVLGGYLRLSRSCLAKGSPERHHKQLKISFSETALETTYQYPSESSVLEELGPEPEVPSAPNPAAQPDDEEDEEELLLLQPELQGGLRTKALIVDESCRR

SEQID No:300

MSEHVEPAAPGPGPNGGGGGPAPARGPRTPNLNPNPLINVRDRLFHALFFKMAVTYS
RLFPPAFRRLFEFFVLLKALFVLFVLAYIHIVFSRSPINCLEHVRDKWPREGILRVEVRHN
SSRAPVFLQFCDSGGRGSFPGLAVEPGSNLDMEDEEEEELTMEMFGNSSIKFELDIEP
KVFKPPSSTEALNDSQEFPFPETPTKVWPQDEYIVEYSLEYGFLRLSQATRQRLSIPVM
VVTLDPTRDQCFGDRFSRLLLDEFLGYDDILMSSVKGLAENEENKGFLRNVVSGEHYRF
VSMWMARTSYLAAFAIMVIFTLSVSMLLRYSHHQIFVFIVDLLQMLEMNMAIAFPAAPLLT
VILALVGMEAIMSEFFNDTTTAFYIILIVWLADQYDAICCHTSTSKRHWLRFFYLYHFAFYA
YHYRFNGQYSSLALVTSWLFIQHSMIYFFHHYELPAILQQVRIQEMLLQAPPLGPGTPTA
LPDDMNNNSGAPATAPDSAGQPPALGPVFELVSKERGWGSAEGSGGVLVGLQ

SEQID No:301

KEQSELDQDLDDVEEVEEEETGEETKLKARQLTVQMMQNPQILAALQERLDGLVETPT GYIESLPRVVKRRVNALKNLQVKCAQIEAKFYEEVHDLERKYAVLYQPLFDKRFEIINAIY EPTEEECEWKPDEEDEISEELKEKAKIEDEKKDEEKEDPKGIPEFWLTVFKNVDLLSDM VQEHDEPILKHLKDIKVKFSDAGQPMSFVLEFHFEPNEYFTNEVLTKTYRMRSEPDDSD PFSFDGPEIMGCTGCQIDWKKGKNVTLKTIKKKQKHKGRGTVRTVTKTVSNDSFFNFFA PPEVIPKFSAFDDDAEAILAADFEIGHFLRERIIPRSVLYFTGEAIEDDDDDDYDEEGEEAD EGYQLFEEVKSCSKLFQRWLQ

SEQID No:302

GKQNSKLRPEVMQDLLESTDFTEHEIQEWYKGFLRDCPSGHLSMEEFKKIYGNFFPYG DASKFAEHVFRTFDANGDGTIDFREFIIALSVTSRGKLEQKLKWAFSMYDLDGNGYISKA EMLEIVQAIYKMVSSVMKMPEDESTPEKRTEKIFRQMDTNRDGKLSLEEFIRGAKSDPSI VRLLQCDPSSAGQF

SEQID No:303

MVEKGPEVSGKRRGRNNAAASAAAASAAASAACASPAATAASGAAASSASAAAAS AAAAPNNGQNKSLAAAAPNGNSSSNSWEEGSSGSSSDEEHGGGGMRVGPQYQAVV PDFDPAKLARRSQERDNLGMLVWSPNQNLSEAKLDEYIAIAKEKHGYNMEQALGMLFW HKHNIEKSLADLPNFTPFPDEWTVEDKVLFEQAFSFHGKTFHRIQQMLPDKSIASLVKFY YSWKKTRTKTSVMDRHARKQKREREESEDELEEANGNNPIDIEVDQNKESKKEVPPTE TVPQVKKEKHSTQAKNRAKRKPPKGMFLSQEDVEAVSANATAATTVLRQLDMELVSVK RQIQNIKQTNSALKEKLDGGIEPYRLPEVIQKCNARWTTEEQLLAVQAIRKYGRDFQAIS DVIGNKSVVQVKNFFVNYRRRFNIDEVLQEWEAEHGKEETNGPSNQKPVKSPDNSIKM PEEEDEAPVLDVRYASAS

SEQID No:304

MSELEKAMVALIDVFHQYSGREGDKHKLKKSELKELINNELSHFLEEIKEQEVVDKVMET LDNDGDGECDFQEFMAFVAMVTTACHEFFEHE

SEQID No:305

MDDDIAALVVDNGSGMCKAGFAGDDAPRAVFPSIVGRPRHQGVMVGMGQKDSYVGD EAQSKRGILTLKYPIEHGIVTNWDDMEKIWHHTFYNELRVAPEEHPVLLTEAPLNPKANR EKMTQIMFETFNTPAMYVAIQAVLSLYASGRTTGIVMDSGDGVTHTVPIYEGYALPHAIL RLDLAGRDLTDYLMKILTERGYSFTTTAEREIVRDIKEKLCYVALDFEQEMATAASSSSL EKSYELPDGQVITIGNERFRCPEALFQPSFLGMESCGIHETTFNSIMKCDVDIRKDLYAN TVLSGGTTMYPGIADRMQKEITALAPSTMKIKIIAPPERKYSVWIGGSILASLSTFQQMWI SKQEYDESGPSIVHRKCF

SEQID No:306

MRECISIHVGQAGVQIGNACWELYCLEHGIQPDGQMPSDKTIGGGDDSFNTFFSETGA
GKHVPRAVFVDLEPTVIDEVRTGTYRQLFHPEQLITGKEDAANNYARGHYTIGKEIIDLVL
DRIRKLADQCTGLQGFLVFHSFGGGTGSGFTSLLMERLSVDYGKKSKLEFSIYPAPQVS
TAVVEPYNSILTTHTTLEHSDCAFMVDNEAIYDICRRNLDIERPTYTNLNRLISQIVSSITA
SLRFDGALNVDLTEFQTNLVPYPRIHFPLATYAPVISAEKAYHEQLSVAEITNACFEPAN
QMVKCDPRHGKYMACCLLYRGDVVPKDVNAAIATIKTKRSIQFVDWCPTGFKVGINYQ
PPTVVPGGDLAKVQRAVCMLSNTTAIAEAWARLDHKFDLMYAKRAFVHWYVGEGMEE
GEFSEAREDMAALEKDYEEVGVDSVEGEGEEEGEEY

SEQID No:307

MREIVHIQAGQCGNQIGAKFWEVISDEHGIDPTGTYHGDSDLQLDRISVYYNEATGGKY VPRAILVDLEPGTMDSVRSGPFGQIFRPDNFVFGQSGAGNNWAKGHYTEGAELVDSVL DVVRKEAESCDCLQGFQLTHSLGGGTGSGMGTLLISKIREEYPDRIMNTFSVVPSPKVS DTVVEPYNATLSVHQLVENTDETYCIDNEALYDICFRTLKLTTPTYGDLNHLVSATMSGV TTCLRFPGQLNADLRKLAVNMVPFPRLHFFMPGFAPLTSRGSQQYRALTVPELTQQVF DAKNMMAACDPRHGRYLTVAAVFRGRMSMKEVDEQMLNVQNKNSSYFVEWIPNNVK TAVCDIPPRGLKMAVTFIGNSTAIQELFKRISEQFTAMFRRKAFLHWYTGEGMDEMEFT EAESNMNDLVSEYQQYQDATAEEEEDFGEEAEEEA

SEQID No:308

MEGSLEREAPAGALAAVLKHSSTLPPESTQVRGYDFNRGVNYRALLEAFGTTGFQATN FGRAVQQVNAMIEKKLEPLSQDEDQHADLTQSRRPLTSCTIFLGYTSNLISSGIRETIRYL VQHNMVDVLVTTAGGVEEDLIKCLAPTYLGEFSLRGKELRENGINRIGNLLVPNENYCKF EDWLMPILDQMVMEQNTEGVKWTPSKMIARLGKEINNPESVYYWAQKNHIPVFSPALT DGSLGDMIFFHSYKNPGLVLDIVEDLRLINTQAIFAKCTGMIILGGGVVKHHIANANLMRN GADYAVYINTAQEFDGSDSGARPDEAVSWGKIRVDAQPVKVYADASLVFPLLVAETFA QKMDAFMHEKNED

SEQID No:309

MADPKYADLPGIARNEPDVYETSDLPEDDQAEFDAEELTSTSVEHIIVNPNAAYDKFKDK RVGTKGLDFSDRIGKTKRTGYESGEYEMLGEGLGVKETPQQKYQRLLHEVQELTTEVE KIKTTVKESATEEKLTPVLLAKQLAALKQQLVASHLEKLLGPDAAINLTDPDGALAKRLLL QLEATKNSKGGSGGKTTGTPPDSSLVTYELHSRPEQDKFSQAAKVAELEKRLTELETA VRCDQDAQNPLSAGLQGACLMETVELLQAKVSALDLAVLDQVEARLQSVLGKVNEIAK HKASVEDADTQSKVHQLYETIQRWSPIASTLPELVQRLVTIKQLHEQAMQFGQLLTHLD TTQQMIANSLKDNTTLLTQVQTTMRENLATVEGNFASIDERMKKLGK

SEQID No:310

MRKETPPPLVPPAAREWNLPPNAPACMERQLEAARYRSDGALLLGASSLSGRCWAGS LWLFKDPCAAPNEGFCSAGVQTEAGVADLTWVGERGILVASDSGAVELWELDENETLI VSKFCKYEHDDIVSTVSVLSSGTQAVSGSKDICIKVWDLAQQVVLSSYRAHAAQVTCVA ASPHKDSVFLSCSEDNRILLWDTRCPKPASQIGCSAPGYLPTSLAWHPQQSEVFVFGD ENGTVSLVDTKSTSCVLSSAVHSQCVTGLVFSPHSVPFLASLSEDCSLAVLDSSLSELF RSQAHRDFVRDATWSPLNHSLLTTVGWDHQVVHHVVPTEPLPAPGPASVTE

SEQID No:311

MSISSDEVNFLVYRYLQESGFSHSAFTFGIESHISQSNINGALVPPAALISIIQKGLQYVEA EVSINEDGTLFDGRPIESLSLIDAVMPDVVQTRQQAYRDKLAQQQAAAAAAAAAAAAAAQQ GSAKNGENTANGEENGAHTIANNHTDMMEVDGDVEIPPNKAVVLRGHESEVFICAWNP VSDLLASGSGDSTARIWNLSENSTSGSTQLVLRHCIREGGQDVPSNKDVTSLDWNSEG TLLATGSYDGFARIWTKDGNLASTLGQHKGPIFALKWNKKGNFILSAGVDKTTIIWDAHT GEAKQQFPFHSAPALDVDWQSNNTFASCSTDMCIHVCKLGQDRPIKTFQGHTNEVNAI KWDPTGNLLASCSDDMTLKIWSMKQDNCVHDLQAHNKEIYTIKWSPTGPGTNNPNANL MLASASFDSTVRLWDVDRGICIHTLTKHQEPVYSVAFSPDGRYLASGSFDKCVHIWNTQ TGALVHSYRGTGGIFEVCWNAAGDKVGASASDGSVCVLDLRK

SEQID No:312

MDEKVFTKELDQWIEQLNECKQLSESQVKSLCEKAKEILTKESNVQEVRCPVTVCGDV HGQFHDLMELFRIGGKSPDTNYLFMGDYVDRGYYSVETVTLLVALKVRYRERITILRGN HESRQITQVYGFYDECLRKYGNANVWKYFTDLFDYLPLTALVDGQIFCLHGGLSPSIDTL DHIRALDRLQEVPHEGPMCDLLWSDPDDRGGWGISPRGAGYTFGQDISETFNHANGL TLVSRAHQLVMEGYNWCHDRNVVTIFSAPNYCYRCGNQAAIMELDDTLKYSFLQFDPA PRRGEPHVTRRTPDYFL

SEQID No:313

MDDKAFTKELDQWVEQLNECKQLNENQVRTLCEKAKEILTKESNVQEVRCPVTVCGDV HGQFHDLMELFRIGGKSPDTNYLFMGDYVDRGYYSVETVTLLVALKVRYPERITILRGN HESRQITQVYGFYDECLRKYGNANVWKYFTDLFDYLPLTALVDGQIFCLHGGLSPSIDTL DHIRALDRLQEVPHEGPMCDLLWSDPDDRGGWGISPRGAGYTFGQDISETFNHANGL TLVSRAHQLVMEGYNWCHDRNVVTIFSAPNYCYRCGNQAAIMELDDTLKYSFLQFDPA PRRGEPHVTRRTPDYFL

SEQID No:314

AAADGDDSLYPIAVLIDELRNEDVQLRLNSIKKLSTIALALGVERTRSELLPFLTDTIYDED EVLLALAEQLGTFTTLVGGPEYVHCLLPPLESLATVEETVVRDKAVESLRAISHEHSPSD LEAHFVPLVKRLAGGDWFTSRTSACGLFSVCYPRVSSAVKAELRQYFRNLCSDDTPMV RRAAASKLGEFAKVLELDNVKSEIIPMFSNLASDEQDSVRLLAVEACVNIAQLLPQEDLE ALVMPTLRQAAEDKSWAVRYMVADKFTELQKAVGPEITKTDLVPAFQNLMKDCEAEVR AAASHKVKEFCENLSADCRENVIMSQILPCIKELVSDANQHVKSALASVIMGLSPILGKD NTIEHLLPLFLAQLKDECPEVRLNIISNLDCVNEVIGIRQLSQSLLPAIVELAEDAKWRVRL AIIEYMPLLAGQLGVEFFDEKLNSLCMAWLVDHVYAIREAATSNLKKLVEKFGKEWAHA TIIPKVLAMSGDPNYLHRMTTLFCINVLSEVCGQDITTKHMLPTVLRMAGDPVANVRFNV AKSLQKIGPILDNSTLQSEVKPILEKLTQDQDVDVKYFAQEALTVLSLA

SEQID No:315

MAEPRQEFEVMEDHAGTYGLGDRKDQGGYTMHQDQEGDTDAGLKESPLQTPTEDGS EEPGSETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHTEIPEGTTAEEAGIGDTPSLE DEAAGHVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPRGAAPPGQKGQANATRIP AKTPPAPKTPPSSGEPPKSGDRSGYSSPGSPGTPGSRSRTPSLPTPPTREPKKVAVVR TPPKSPSSAKSRLQTAPVPMPDLKNVKSKIGSTENLKHQPGGGKVQIINKKLDLSNVQS KCGSKDNIKHVPGGGSVQIVYKPVDLSKVTSKCGSLGNIHHKPGGGQVEVKSEKLDFK DRVQSKIGSLDNITHVPGGGNKKIETHKLTFRENAKAKTDHGAEIVYKSPVVSGDTSPR HLSNVSSTGSIDMVDSPQLATLADEVSASLAKQGL

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